



# STIC Search Report

## Biotech-Chem Library

STIC Database Tracking Number: 208368

TO: Ralph J Gitomer  
Location: REM/3D65/3C70  
Art Unit: 1657  
Friday, December 15, 2006

Case Serial Number: 10/801931

From: Mary Jane Ruhl  
Location: Biotech-Chem Library  
Remsen 1-A-62  
Phone: 571-272-2524

maryjane.ruhl@uspto.gov

### Search Notes

Examiner Gitomer,

Here are the results for your recent search request. These results should be available in SCORE in approximately one day.

To access SCORE, click on the link: <http://es/ScoreAccessWeb>

Type SN in Identification Number box -> submit

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For Structure or Text searches, click on the Number of Mega Items.

Click on Download.

Please feel free to contact me if you have any questions about these results.

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Sincerely,

Mary Jane Ruhl  
Technical Information Specialist  
STIC  
Remsen 1-A-61  
Ext. 22524



## SEARCH HISTORY

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(FILE 'HOME' ENTERED AT 12:09:00 ON 15 DEC 2006)

FILE 'HCAPLUS' ENTERED AT 12:11:15 ON 15 DEC 2006

E KOLLER MANFRED R/AU  
L1 32 SEA ABB=ON ("KOLLER MANFRED R"/AU OR "KOLLER MANFRED"/AU OR  
"KOLLER MANFRED R"/AU OR "KOLLER MANFRED ROBERT"/AU)  
E HANANIA ELIE G/AU  
L2 24 SEA ABB=ON ("HANANIA E G"/AU OR "HANANIA ELIE"/AU OR "HANANIA  
ELIE G"/AU OR "HANANIA ELIE GEORGE"/AU OR "HANANIA ELLIE  
G"/AU)  
E FIECK ANNABETH/AU  
L3 8 SEA ABB=ON "FIECK ANNABETH"/AU  
E EISFELD TIMOTHY M/AU  
L4 11 SEA ABB=ON ("EISFELD TIMOTHY"/AU OR "EISFELD TIMOTHY M"/AU)  
L5 1 SEA ABB=ON L1 AND L2 AND L3 AND L4  
L6 ANALYZE L5 1 CT : 14 TERMS  
L7 255033 SEA ABB=ON ?CELL? AND ?PURIF?  
L8 5930 SEA ABB=ON L7 AND ?IMMOBILIZ?  
L9 5930 SEA ABB=ON L8 AND (?IMMOBILIZ? OR ?DESTROY? OR ?KILL?)  
L10 359 SEA ABB=ON L9 AND ?SECRET?  
L11 43 SEA ABB=ON L10 AND (?IMAG? OR ?RADIAT? OR ?LIGHT?)  
L12 10 SEA ABB=ON L11 AND ?METHOD?  
L13 43 SEA ABB=ON L11 OR L12  
L14 38 SEA ABB=ON L13 AND (PRD<20040315 OR PD<20040315)

FILE 'MEDLINE, BIOSIS, EMBASE, JAPIO, JICST-EPLUS, WPIDS' ENTERED AT  
12:21:29 ON 15 DEC 2006

L15 155 SEA ABB=ON L13  
L16 98 DUP REMOV L15 (57 DUPLICATES REMOVED)  
L17 55 SEA ABB=ON L16 AND ?METHOD?  
L18 0 SEA ABB=ON L17 AND DRUG?(W) SCREEN?  
L19 16 SEA ABB=ON L17 AND SCREEN?  
L20 19 SEA ABB=ON L17 AND GEL?

FILE 'HCAPLUS' ENTERED AT 12:24:46 ON 15 DEC 2006

L21 11 SEA ABB=ON L14 AND GEL?  
L22 38 SEA ABB=ON L14 OR L21 — *not all have "gel"*

FILE HOME

FILE HCAPLUS

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FILE COVERS 1907 - 15 Dec 2006 VOL 145 ISS 26  
FILE LAST UPDATED: 14 Dec 2006 (20061214/ED)

New CAS Information Use Policies, enter HELP USAGETERMS for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

## FILE MEDLINE

FILE LAST UPDATED: 14 Dec 2006 (20061214/UP). FILE COVERS 1950 TO DATE.

In preparation for the annual MEDLINE reload, the National Library of Medicine (NLM) has suspended delivery of regular updates as of November 15, 2006. In-process and in-data-review records will resume delivery on November 21, 2006, and will continue to be added to MEDLINE until December 17, 2006.

On December 17, 2006, all regular MEDLINE updates from November 15 to December 16 will be added to MEDLINE, along with 2007 Medical Subject Headings (MeSH(R)) and 2007 tree numbers.

The annual reload will be available in early 2007.

This file contains CAS Registry Numbers for easy and accurate substance identification.

## FILE BIOSIS

FILE COVERS 1969 TO DATE.

CAS REGISTRY NUMBERS AND CHEMICAL NAMES (CNs) PRESENT FROM JANUARY 1969 TO DATE.

RECORDS LAST ADDED: 14 December 2006 (20061214/ED)

## FILE EMBASE

FILE COVERS 1974 TO 15 Dec 2006 (20061215/ED)

EMBASE is now updated daily. SDI frequency remains weekly (default) and biweekly.

This file contains CAS Registry Numbers for easy and accurate substance identification.

## FILE JAPIO

FILE LAST UPDATED: 12 DEC 2006 <20061212/UP>

FILE COVERS APRIL 1973 TO AUGUST 31, 2006

>>> GRAPHIC IMAGES AVAILABLE <<<

>>> NEW IPC8 DATA AND FUNCTIONALITY NOW AVAILABLE IN FILE JAPIO.

SEE HELP CHANGE

AND

[http://www.stn-international.de/stndatabases/details/ipc\\_reform.html](http://www.stn-international.de/stndatabases/details/ipc_reform.html) <<<

## FILE JICST-EPLUS

FILE COVERS 1985 TO 12 DEC 2006 (20061212/ED)

THE JICST-EPLUS FILE HAS BEEN RELOADED TO REFLECT THE 1999 CONTROLLED TERM (/CT) THESAURUS RELOAD.

## FILE WPIDS

FILE LAST UPDATED: 8 DEC 2006 <20061208/UP>

MOST RECENT THOMSON SCIENTIFIC UPDATE: 200679 <200679/DW>

DERWENT WORLD PATENTS INDEX SUBSCRIBER FILE, COVERS 1963 TO DATE

>>> YOU ARE IN THE NEW AND ENHANCED DERWENT WORLD PATENTS INDEX <<<

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<http://scientific.thomson.com/support/patents/coverage/latestupdates/>

PLEASE BE AWARE OF THE NEW IPC REFORM IN 2006, SEE  
[http://www.stn-international.de/stndatabases/details/ipc\\_reform.html](http://www.stn-international.de/stndatabases/details/ipc_reform.html) and  
<http://scientific.thomson.com/media/scpdf/ipcrdwpi.pdf>

>>> FOR DETAILS ON THE NEW AND ENHANCED DERWENT WORLD PATENTS INDEX  
PLEASE SEE

[http://www.stn-international.de/stndatabases/details/dwpi\\_r.html](http://www.stn-international.de/stndatabases/details/dwpi_r.html) <<<

>>> YOU ARE IN THE NEW AND ENHANCED DERWENT WORLD PATENTS INDEX <<<

10801931

## INVENTOR SEARCH

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L5 ANSWER 1 OF 1 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:1004274 HCAPLUS

DOCUMENT NUMBER: 143:263091

TITLE: Methods for purification of cells based on product secretion using immobilization, imaging and radiation

INVENTOR(S): Koller, Manfred R.; Hanania, Elie G.  
; Fieck, Annabeth; Eisfeld, Timothy  
M.

PATENT ASSIGNEE(S): USA

SOURCE: U.S. Pat. Appl. Publ., 18 pp.

CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

## PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2005202558	A1	20050915	US 2004-801931	20040315
AU 2005224624	A1	20050929	AU 2005-224624	20050314
CA 2559736	AA	20050929	CA 2005-2559736	20050314
WO 2005090555	A1	20050929	WO 2005-US8347	20050314

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

EP 1725653	A1	20061129	EP 2005-727754	20050314
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R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR

PRIORITY APPLN. INFO.: US 2004-801931 A 20040315  
WO 2005-US8347 W 20050314

AB The invention provides methods for purifying one or more cells based on the level of one or more products secreted by the cells. In one embodiment, the method involves (a) contacting a plurality of cells immobilized in proximity to a capture matrix, the capture matrix capable of localizing a product secreted by one or more of the cells, with an agent that selectively binds to the product, the agent capable of generating a signal detectable as a property of light; (b) illuminating a population of the cells, the population contained in a frame; (c) detecting two or more properties of light directed from the frame, wherein a first property of light identifies substantially all cells of the population, and the second property of light identifies product localized to the capture matrix; (d) locating (i) substantially all cells of the population with reference to the detected first property of light, and (ii) one or more selected cells with reference to the detected second property of light, and (e) irradiating the non-selected cells, wherein each non-selected cell

receives a substantially LD of radiation, whereby one or more selected cells having a desired product secretion profile are purified.

IC ICM C12N005-00

ICS C12N005-02

INCL 435378000; 435383000

CC 9-11 (Biochemical Methods)

Section cross-reference(s): 1

ST cell purifn immobilization radiation imaging

IT Proteins

RL: BSU (Biological study, unclassified); BIOL (Biological study)

(A; methods for purification of cells based on product secretion using immobilization, imaging and radiation)

IT Proteins

RL: BSU (Biological study, unclassified); BIOL (Biological study)

(G; methods for purification of cells based on product secretion using immobilization, imaging and radiation)

IT Antibodies and Immunoglobulins

RL: BSU (Biological study, unclassified); BIOL (Biological study)

(fragments; methods for purification of cells based on product secretion using immobilization, imaging and radiation)

IT Animal cell line

Cell

Drug screening

Imaging

Immobilization, molecular or cellular

Radiation

(methods for purification of cells based on product secretion using immobilization, imaging and radiation)

IT Antibodies and Immunoglobulins

Cytokines

Enzymes, biological studies

Growth factors, animal

Hormones, animal, biological studies

Neurotransmitters

Peptides, biological studies

RL: BSU (Biological study, unclassified); BIOL (Biological study)

(methods for purification of cells based on product secretion using immobilization, imaging and radiation)

IT Proteins

RL: BSU (Biological study, unclassified); BIOL (Biological study)

(signaling; methods for purification of cells based on product secretion using immobilization, imaging and radiation)

IT Proteins

RL: BSU (Biological study, unclassified); BIOL (Biological study)

(therapeutic; methods for purification of cells based on product secretion using immobilization, imaging and radiation)

## SEARCH IN HCAPLUS

=&gt; d que stat 122

L7 255033 SEA FILE=HCAPLUS ABB=ON ?CELL? AND ?PURIF?  
L8 5930 SEA FILE=HCAPLUS ABB=ON L7 AND ?IMMOBILIZ?  
L9 5930 SEA FILE=HCAPLUS ABB=ON L8 AND (?IMMOBILIZ? OR ?DESTROY? OR  
?KILL?)  
L10 359 SEA FILE=HCAPLUS ABB=ON L9 AND ?SECRET?  
L11 43 SEA FILE=HCAPLUS ABB=ON L10 AND (?IMAG? OR ?RADIAT? OR  
?LIGHT?)  
L12 10 SEA FILE=HCAPLUS ABB=ON L11 AND ?METHOD?  
L13 43 SEA FILE=HCAPLUS ABB=ON L11 OR L12  
L14 38 SEA FILE=HCAPLUS ABB=ON L13 AND (PRD<20040315 OR PD<20040315)  
  
L21 11 SEA FILE=HCAPLUS ABB=ON L14 AND GEL?  
L22 38 SEA FILE=HCAPLUS ABB=ON L14 OR L21

=&gt; d ibib abs 122 1-38

L22 ANSWER 1 OF 38 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:1292638 HCAPLUS

DOCUMENT NUMBER: 144:33522

TITLE: Substrate-binding, catalytically inactive hydrolases  
as carriers for the **immobilization** of fusion  
proteinsINVENTOR(S): Darzins, Aldis; Encell, Lance; Johnson, Tonny;  
Klaubert, Dieter; Los, Georgyi V.; Mcdougall, Mark;  
Wood, Keith V.; Wood, Monika G.; Zimprich, Chad

PATENT ASSIGNEE(S): USA

SOURCE: U.S. Pat. Appl. Publ., 121 pp., Cont.-in-part of U.S.  
Ser. No. 768,976.

CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2005272114	A1	20051208	US 2004-6031	20041206 <--
US 2004214258	A1	20041028	US 2004-768976	20040130 <--
US 2006024808	A1	20060202	US 2005-194110	20050729
WO 2006093529	A2	20060908	WO 2005-US27307	20050729

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,  
CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,  
GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ,  
LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA,  
NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK,  
SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU,  
ZA, ZM, ZW

RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,  
IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ,  
CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH,  
GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,  
KG, KZ, MD, RU, TJ, TM

PRIORITY APPLN. INFO.:

US 2003-444094P	P	20030131 <--
US 2003-474659P	P	20030530 <--
US 2004-768976	A2	20040130 <--
US 2004-592499P	P	20040730

. US 2004-6031

A 20041206

OTHER SOURCE(S): MARPAT 144:33522

AB Hydrolase variants that retain substrate binding, and capable of forming a covalent bond with a substrate, but lacking the catalytic activity to release the hydrolysis products are described for use in the **immobilization** of proteins onto surfaces carrying a substrate for the hydrolase are described. The binding of the hydrolase to substrate is more stable than that of the wild type enzyme. The catalytically inactive variant has at least two amino acid substitutions. Substrates for hydrolases comprising one or more functional groups are also provided, as well as **methods** of using the mutant hydrolase and the substrates of the invention. Also provided is a fusion protein capable of forming a stable bond with a substrate and **cells** which express the fusion protein. Development of a catalytically inactive variant of the haloalkane dehalogenase of *Rhodococcus rhodochrous* is demonstrated. Use of fusion products with fluorescent proteins and enzymes in **imaging** in vivo are demonstrated.

L22 ANSWER 2 OF 38 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:239381 HCAPLUS

DOCUMENT NUMBER: 140:284819

TITLE: pH-induced Conversion of the Transport Lectin ERGIC-53 Triggers Glycoprotein Release

AUTHOR(S): Appenzeller-Herzog, Christian; Roche, Annie-Claude; Nufer, Oliver; Hauri, Hans-Peter

CORPORATE SOURCE: Biozentrum, University of Basel, Basel, CH-4056, Switz.

SOURCE: Journal of Biological Chemistry (2004), 279(13), 12943-12950

CODEN: JBCHA3; ISSN: 0021-9258

PUBLISHER: American Society for Biochemistry and Molecular Biology

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The recycling mannose lectin ERGIC-53 operates as a transport receptor by mediating efficient endoplasmic reticulum (ER) export of some **secretory** glycoproteins. Binding of cargo to ERGIC-53 in the ER requires Ca<sup>2+</sup>. Cargo release occurs in the ERGIC, but the mol. mechanism is unknown. Here we report efficient binding of **purified** ERGIC-53 to **immobilized** mannose at pH 7.4, the pH of the ER, but not at **slightly** lower pH. PH sensitivity of the lectin was more prominent when Ca<sup>2+</sup> concns. were low. A conserved histidine in the center of the carbohydrate recognition domain was required for lectin activity suggesting it may serve as a mol. pH/Ca<sup>2+</sup> sensor. Acidification of **cells** inhibited the association of ERGIC-53 with the known cargo cathepsin Z-related protein and dissociation of this glycoprotein in the ERGIC was impaired by organelle neutralization that did not impair the transport of a control protein. The results elucidate the mol. mechanism underlying reversible lectin/cargo interaction and establish the ERGIC as the earliest low pH site of the **secretory** pathway.

REFERENCE COUNT: 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L22 ANSWER 3 OF 38 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:60033 HCAPLUS

DOCUMENT NUMBER: 140:110128

TITLE: Dendritic **cell** function and immune response potentiation with a **purified** mol. that binds specifically to **cell** surface B7-DC polypeptides



INVENTOR(S): Pease, Larry R.; Rodriguez, Moses; Ure, Daren; Nguyen, Loc T.; Radhakrishnan, Suresh  
 PATENT ASSIGNEE(S): Mayo Foundation for Medical Education and Research, USA  
 SOURCE: U.S. Pat. Appl. Publ., 26 pp.  
 CODEN: USXXCO  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004014207	A1	20040122	US 2002-196601	20020716 <--
US 7052694	B2	20060530		
WO 2004007679	A2	20040122	WO 2003-US21933	20030715 <--
WO 2004007679	A3	20041014		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2003253897	A1	20040202	AU 2003-253897	20030715 <--
EP 1543037	A2	20050622	EP 2003-764607	20030715 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
US 2005249737	A1	20051110	US 2005-178160	20050708 <--
PRIORITY APPLN. INFO.:				
			US 2002-196601	A1 20020716 <--
			WO 2003-US21933	W 20030715 <--

AB A mol. capable of potentiating immune responses is described, as well as **methods** for using the mol. to enhance immune responses and enhance dendritic **cell** function. Preferably, the mol. is a human serum-derived antibody (sHIgM12). This antibody was shown to potentiate the antigen-presenting function of dendritic **cells**. In a mouse model of B16 melanoma the sHIgM12 treatment was protective against lethal tumor challenge, it inhibited the tumor growth, and mice displayed persistent antitumor resistance. The inventors also produced a recombinant human IgM antibody (sHIgM22) and the same **method** was used to generate a recombinant supply of sHIgM12. Also described are compns. containing the mol. and **methods** for using the compns. to treat or immunize individuals.

REFERENCE COUNT: 77 THERE ARE 77 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L22 ANSWER 4 OF 38 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2003:810633 HCAPLUS

DOCUMENT NUMBER: 140:58520

TITLE: Large-scale transient transfection of serum-free suspension-growing HEK293 EBNA1 **cells**:  
 Peptone additives improve **cell** growth and transfection efficiency

AUTHOR(S): Pham, Phuong Lan; Perret, Sylvie; Doan, Huyen Chau; Cass, Brian; St-Laurent, Gilles; Kamen, Amine; Durocher, Yves

CORPORATE SOURCE: Animal Cell Technology Group, Bioprocess Platform,

SOURCE: Biotechnology Research Institute, National Research Council Canada, Montreal, H4P 2R2, Can.  
Biotechnology and Bioengineering (2003), 84(3), 332-342  
CODEN: BIBIAU; ISSN: 0006-3592  
PUBLISHER: John Wiley & Sons, Inc.  
DOCUMENT TYPE: Journal  
LANGUAGE: English

AB Large-scale transient transfection of mammalian **cells** is a recent and powerful technol. for the fast production of milligram amts. of recombinant proteins (r-proteins). As many r-proteins used for therapeutic and structural studies are naturally **secreted** or engineered to be **secreted**, a cost-effective serum-free culture medium that allows their efficient expression and **purification** is required. In an attempt to design such a serum-free medium, the effect of nine protein hydrolyzates on **cell** proliferation, transfection efficiency, and volumetric productivity was evaluated using green fluorescent protein (GFP) and human placental **secreted** alkaline phosphate (SEAP) as reporter genes. The suspension growing, serum-free adapted HEK293SF-3F6 **cell** line was stably transfected with an EBNA1-expression vector to increase protein expression when using EBV oriP bearing plasmids. Compared to our standard serum-free medium, concomitant addition of the **gelatin** peptone N3 and removal of BSA **slightly** enhanced transfection efficiency and significantly increased volumetric productivity fourfold. Using the optimized medium formulation, transfection efficiencies between 40-60% were routinely obtained and SEAP production reached 18 mg/L-1. To date, we have successfully produced and **purified** over fifteen r-proteins from 1-14-L bioreactors using this serum-free system. As examples, we describe the scale-up of two **secreted** his-tagged r-proteins Tie-2 and Neuropilin-1 **extracellular** domains (ED) in bioreactors. Each protein was successfully **purified** to >95% purity following a single **immobilized** metal affinity chromatog. (IMAC) step. In contrast, **purification** of Tie-2 and Neuropilin-1 produced in serum-containing medium was much less efficient. Thus, the use of our new serum-free EBNA1 **cell** line with peptone-enriched serum-free medium significantly improves protein expression compared to peptone-less medium, and significantly increases their **purification** efficiency compared to serum-containing medium. This eliminates labor-intensive and expensive chromatog. steps, and allows for the simple, reliable, and extremely fast production of milligram amts. of r-proteins within 5 days posttransfection.

REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L22 ANSWER 5 OF 38 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2003:241205 HCAPLUS

DOCUMENT NUMBER: 140:25066

TITLE: O-Glycosylation of a Recombinant Carbohydrate-Binding Module Mutant **Secreted** by Pichia pastoris

AUTHOR(S): Boraston, Alisdair B.; Sandercock, Linda E.; Warren, R. Antony J.; Kilburn, Douglas G.

CORPORATE SOURCE: The Protein Engineering Network of Centres of Excellence, PENCE Inc., Edmonton, Can.

SOURCE: Journal of Molecular Microbiology and Biotechnology (2003), 5(1), 29-36

CODEN: JMMBFF; ISSN: 1464-1801

PUBLISHER: S. Karger AG

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Carbohydrate-binding modules (CBMs; previously called **cellulose** -binding domains) make **excellent** fusion partners for the **immobilization** or **purification** of polypeptides. However, their use in eukaryotic hosts has been limited by glycosylation, which interferes with the ability of the CBM to bind to **cellulose**. We have engineered the C-terminal carbohydrate-binding module from **Cellulomonas fimi** xylanase 10A such that it lacks N-glycosylation sites. This variant, called CBM2aNgly-, was produced and **secreted** by the methylotrophic yeast *Pichia pastoris* and found to be O-glycosylated. The O-linked glycans were composed entirely of mannose in a ratio of 1 mol of mannose to 4 mol of protein. The overall distribution of mannose on the O-glycosylated CBM mutant ranged from 1 to 9 mannose residues with the oligosaccharide sizes ranging from Man1 to Man4. MALDI-TOF (all matrix-assisted-laser-desorption time of **flight**) mass spectrometry (MS) was used to map the O-glycosylation to three regions of the polypeptide, each region having a maximum of 4 mannose residues attached to each. Glycans chemical released from CBM2aNgly- and analyzed by fluorophore-assisted carbohydrate electrophoresis were found to contain  $\alpha$ -1,2-,  $\alpha$ -1,3-, and  $\alpha$ -1,6-linkages. Significantly, the O-glycosylation did not influence binding, making CBM2aNgly- a suitable fusion partner for polypeptides produced in *P. pastoris* and other eukaryotic hosts.

REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L22 ANSWER 6 OF 38 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2003:146092 HCAPLUS

DOCUMENT NUMBER: 138:319441

TITLE: An Interferon- $\gamma$ -binding Protein of Novel Structure Encoded by the Fowlpox Virus

AUTHOR(S): Puehler, Florian; Schwarz, Heike; Waidner, Barbara; Kalinowski, Joern; Kaspers, Bernd; Bereswill, Stefan; Staeheli, Peter

CORPORATE SOURCE: Departments of Virology, University of Freiburg, Freiburg, D-79104, Germany

SOURCE: Journal of Biological Chemistry (2003), 278(9), 6905-6911

CODEN: JBCHA3; ISSN: 0021-9258

PUBLISHER: American Society for Biochemistry and Molecular Biology

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Poxviruses have evolved various strategies to counteract the host immune response, one of which is based on the expression of soluble cytokine receptors. Using various biol. assays, the authors detected a chicken interferon- $\gamma$  (chIFN- $\gamma$ )-neutralizing activity in supernatants of fowlpox virus (FPV)-infected **cells** that could be **destroyed** by trypsin treatment. **Secreted** viral proteins were **purified** by affinity chromatog. using matrix-**immobilized** chIFN- $\gamma$ , followed by two-dimensional **gel** electrophoresis. Matrix-assisted laser desorption/ionization time of **flight** mass spectrometry (MALDI-TOF MS) anal. indicated that the viral IFN- $\gamma$ -binding protein in question was encoded by the FPV gene 016. The chicken IFN- $\gamma$  binding and neutralizing activity of the recombinant FPV016 protein was confirmed using supernatants of **cells** infected with a recombinant vaccinia virus that lacked its own IFN- $\gamma$ -binding protein but instead expressed the FPV016 gene. The FPV016 gene product also neutralized the activity of duck and human IFN- $\gamma$  but failed to neutralize the activity of mouse and rat IFN- $\gamma$ . Unlike previously known **cellular** and poxviral

IFN- $\gamma$  receptors, which all contain fibronectin type III domains, the IFN- $\gamma$ -binding protein of FPV contains an Ig domain. Remarkably, it exhibits no homol. to any known viral or **cellular** protein. Because IFN- $\gamma$  receptors of birds have not yet been characterized at the mol. level, the possibility remains that FPV016 represents a hijacked chicken gene and that avian and mammalian IFN- $\gamma$  receptors have fundamentally different primary structures.

REFERENCE COUNT: 55 THERE ARE 55 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L22 ANSWER 7 OF 38 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2001:560777 HCAPLUS

DOCUMENT NUMBER: 135:238271

TITLE: Functional characterization of recombinant chloroplast signal recognition particle

AUTHOR(S): Groves, Matthew R.; Mant, Alexandra; Kuhn, Audrey; Koch, Joachim; Dubel, Stefan; Robinson, Colin; Sinning, Irmgard

CORPORATE SOURCE: Structural Biology Programme, EMBL, Heidelberg, 69117, Germany

SOURCE: Journal of Biological Chemistry (2001), 276(30), 27778-27786

CODEN: JBCHA3; ISSN: 0021-9258

PUBLISHER: American Society for Biochemistry and Molecular Biology

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The signal recognition particle (SRP) is a ubiquitous system for the targeting of membrane and **secreted** proteins. The chloroplast SRP (cpSRP) is unique among SRPs in that it possesses no RNA and is functional in post-translational as well as co-translational targeting. We have expressed and **purified** the two components of the Arabidopsis thaliana chloroplast signal recognition particle (cpSRP) involved in post-translational transport: cpSRP54 and the chloroplast-specific protein, cpSRP43. Recombinant cpSRP supports the efficient in vitro insertion of pea preLhcb1 into isolated thylakoid membranes. Recombinant cpSRP is a stable heterodimer with a mol. mass of .apprx.100 kDa as determined by anal. ultracentrifugation, **gel** filtration anal., and dynamic **light** scattering. The interactions of the components of the recombinant heterodimer and pea preLhcb1 were probed using an **immobilized** peptide library (pepscan) approach. These data confirm two previously reported interactions with the L18 region and the third transmembrane helix of Lhcb1 and suggest that the interface of the cpSRP43 and cpSRP54 proteins is involved in substrate binding. Addnl., cpSRP components are shown to recognize peptides from the cleavable, N-terminal chloroplast transit peptide of preLhcb1. The interaction of cpSRP43 with cpSRP54 was probed in a similar experiment with a peptide library representing cpSRP54. The C terminus of cpSRP54 is essential for the formation of the stable cpSRP complex and cpSRP43 interacts with distinct regions of the M domain of cpSRP54.

REFERENCE COUNT: 48 THERE ARE 48 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L22 ANSWER 8 OF 38 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2001:520266 HCAPLUS

DOCUMENT NUMBER: 135:236585

TITLE: Ni(II)-based **immobilized** metal ion affinity chromatography of recombinant human prolactin from periplasmic Escherichia coli extracts

AUTHOR(S): Ueda, E. K. M.; Gout, P. W.; Morganti, L.  
CORPORATE SOURCE: Department of Biotechnology, Institute of Nuclear and  
Energy Research (IPEN-CNEN), Sao Paulo, Brazil  
SOURCE: Journal of Chromatography, A (2001),  
922(1-2), 165-175  
CODEN: JCRAEY; ISSN: 0021-9673  
PUBLISHER: Elsevier Science B.V.  
DOCUMENT TYPE: Journal  
LANGUAGE: English

AB A novel, two-step preparative technique is described for the  
**purification** of authentic recombinant human prolactin (rhPRL)  
**secreted** into the periplasm of transformed Escherichia coli  
**cells**. The first step is based on **immobilized** metal ion  
affinity chromatog. of periplasmic extract, using Ni(II) as a relatively  
specific ligand for hPRL in this system. It gives superior resolution and  
yield than established ion-exchange chromatog. Size-exclusion chromatog.  
is used for further **purification** to >99.5% purity. The  
**methodol.** is reproducible, leading to 77% recovery. Identity and  
purity of the rhPRL were demonstrated using sodium dodecylsulfate-  
polyacrylamide electrophoresis, isoelec. focusing, mass spectrometry  
(matrix-assisted laser desorption ionization time-of-flight),  
RIA, RP-HPLC and high-performance size-exclusion chromatog. In the Nb2  
bioassay, the hormone showed a bioactivity of 40.9 IU/mg.

REFERENCE COUNT: 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS  
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L22 ANSWER 9 OF 38 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2001:390150 HCAPLUS

DOCUMENT NUMBER: 136:179920

TITLE: Rapid multiserotype detection of human rhinoviruses on  
optically coated silicon surfaces

AUTHOR(S): Ostroff, R.; Ettinger, A.; La, H.; Rihaneck, M.;  
Zalman, L.; Meador, J.; Patick, A. K.; Worland, S.;  
Polisky, B.

CORPORATE SOURCE: Thermo BioStar, Inc., Boulder, CO, 80301, USA

SOURCE: Journal of Clinical Virology (2001), 21(2),  
105-117

CODEN: JCVIFB; ISSN: 1386-6532

PUBLISHER: Elsevier Science Ireland Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Background: More than 100 immunol. distinct serotypes of human  
rhinoviruses (HRV) have been discovered, making detection of surface  
exposed capsid antigens impractical. However, the non-structural protein  
3C protease (3Cpro) is essential for viral replication and is relatively  
highly conserved among serotypes, making it a potential target for  
diagnostic testing. The thin film biosensor is an assay platform that can  
be formatted into a sensitive immunoassay for viral proteins in clin.  
specimens. The technol. utilizes an optically coated silicon surface to  
convert specific mol. binding events into visual color changes by altering  
the reflective properties of **light** through mol. thin films.  
Objective: To develop a rapid test for detection of HRV by developing  
broadly serotype reactive antibodies to 3Cpro and utilizing them in the  
thin film biosensor format. Study design: Polyclonal antibodies to 3Cpro  
were **purified** and incorporated into the thin film assay. The in  
vitro sensitivity, specificity and multiserotype cross-reactivity of the  
3Cpro assay were tested. Nasal washes from naturally infected individuals  
were also tested to verify that 3Cpro was detectable in clin. specimens.  
Results: The 3Cpro assay is a 28-min, non-instrumented room temperature test  
with a visual limit of detection of 12 pM (picomolar) 3Cpro. In terms of

viral titer, as few as 1000 TCID<sub>50</sub> equivalents of HRV2 were detectable. The assay detected 45/52 (87%) of the HRV serotypes tested but showed no cross-reactivity to common respiratory viruses or bacteria. The thin film assay detected 3Cpro in HRV-infected **cell** culture supernatants coincident with first appearance of cytopathic effect. Data are also presented demonstrating 3Cpro detection from clin. samples collected from HRV-infected individuals. The assay detected 3Cpro in expelled nasal **secretions** from a symptomatic individual on the first day of illness. In addition, 9/11 (82%) concentrated nasal wash specimens from HRV infected children were pos. in the 3Cpro test. Conclusion: We have described a novel, sensitive thin film biosensor for rapid detection of HRV 3Cpro. This test may be suitable for the point of care setting, where rapid HRV diagnostic test results could contribute to clin. decisions regarding appropriate antibiotic or antiviral therapy.

REFERENCE COUNT: 52 THERE ARE 52 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L22 ANSWER 10 OF 38 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2001:137979 HCAPLUS

DOCUMENT NUMBER: 134:322466

TITLE: First isolation of human UDP-D-xylose:proteoglycan core protein  $\beta$ -D-xylosyltransferase **secreted** from cultured JAR choriocarcinoma **cells**

AUTHOR(S): Kuhn, Joachim; Gotting, Christian; Schnolzer, Martina; Kempf, Tore; Brinkmann, Thomas; Kleesiek, Knut

CORPORATE SOURCE: Institut fur Laboratoriums- und Transfusionsmedizin, Herz- und Diabeteszentrum Nordrhein-Westfalen, Universitätsklinik der Ruhr-Universität Bochum, Bad Oeynhausen, 32545, Germany

SOURCE: Journal of Biological Chemistry (2001), 276(7), 4940-4947

CODEN: JBCHA3; ISSN: 0021-9258

PUBLISHER: American Society for Biochemistry and Molecular Biology

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Human UDP-D-xylose:proteoglycan core protein  $\beta$ -D-xylosyltransferase (EC 2.4.2.26, XT) initiates the biosynthesis of glycosaminoglycan lateral chains in proteoglycans by transfer of xylose from UDP-xylose to specific serine residues of the core protein. In this study, we report the first isolation of the XT and present the first partial amino acid sequence of this enzyme. We **purified** XT 4,700-fold with 1% yield from serum-free JAR choriocarcinoma **cell** culture supernatant. The isolation procedure included a combination of ammonium sulfate precipitation, heparin affinity chromatog., ion exchange chromatog., and protamine affinity chromatog. Among other proteins an unknown protein was detected by matrix-assisted laser desorption ionization mass spectrometry-time of **flight** anal. in the **purified** sample. The mol. mass of this protein was determined as 120 kDa by SDS-polyacrylamide **gel** electrophoresis. The isolated protein was enzymically cleaved by trypsin and endoproteinase Lys-C. Eleven peptide fragments were sequenced by Edman degradation. Searches with the amino acid sequences in protein and EST data bases showed no homol. to known sequences. XT was enriched by immunoaffinity chromatog. with an **immobilized** antibody against a synthetic peptide deduced from the sequenced peptide fragments and was specifically eluted with the antigen. In addition, XT was **purified** alternatively with an aprotinin affinity chromatog. and was detected by Western blot anal. in the enzyme-containing fraction.

REFERENCE COUNT: 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS

## RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L22 ANSWER 11 OF 38 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2000:898292 HCAPLUS

DOCUMENT NUMBER: 134:161855

TITLE: Costimulation **light**: activation of CD4+ T **cells** with CD80 or CD86 rather than anti-CD28 leads to a Th2 cytokine profile

AUTHOR(S): Broeren, Chris P. M.; Gray, Gary S.; Carreno, Beatriz M.; June, Carl H.

CORPORATE SOURCE: Naval Medical Research Institute, Bethesda, MD, 20814, USA

SOURCE: Journal of Immunology (2000), 165(12), 6908-6914

CODEN: JOIMA3; ISSN: 0022-1767

PUBLISHER: American Association of Immunologists

DOCUMENT TYPE: Journal

LANGUAGE: English

AB To examine the role of CD28 and CTLA-4 in Th **cell** differentiation, we used a novel microsphere-based system to compare the effects of CD28 ligation by Ab or CD80/CD86. One set of beads was prepared by coating with anti-CD3 and anti-CD28 Ab. Another set of beads was prepared by **immobilizing** anti-CD3 and murine CD80-Ig fusion protein or murine CD86-Ig fusion protein on the beads. The three sets of beads were compared in their effects on the ability to activate and differentiate splenic CD4 T **cells**. When **purified** naive CD4+ **cells** were stimulated in vitro, robust proliferation of similar magnitude was induced by all three sets of beads. When cytokine **secretion** was examined, all bead preps. induced an equivalent accumulation of IL-2. In contrast, there was a marked difference in the cytokine **secretion** pattern of the Th2 cytokines IL-4, IL-10, and IL-13. The B7-Ig-stimulated cultures had high concns. of Th2 cytokines, whereas there were low or undetectable concns. in the anti-CD28-stimulated cultures. Addition of anti-CTLA-4 Fab augmented B7-mediated IL-4 **secretion**. These studies demonstrate that B7 is a critical and potent stimulator of Th2 differentiation, and that anti-CD28 prevents this effect.

REFERENCE COUNT: 48 THERE ARE 48 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L22 ANSWER 12 OF 38 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2000:30883 HCAPLUS

DOCUMENT NUMBER: 132:235599

TITLE: Three-step **purification** of bacterially expressed human single-chain Fv antibodies for clinical applications

AUTHOR(S): Laroche-Traineau, J.; Clofent-Sanchez, G.; Santarelli, X.

CORPORATE SOURCE: CNRS, Laboratoire de Pathologie Cellulaire de l'Hemostase, Pessac, 33604, Fr.

SOURCE: Journal of Chromatography, B: Biomedical Sciences and Applications (2000), 737(1 + 2), 107-117

CODEN: JCBEBP; ISSN: 0378-4347

PUBLISHER: Elsevier Science B.V.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The authors have obtained a **cell** line which **secretes** a human monoclonal IgM (B7) reacting with the myosin heavy chain of human heart. The authors have constructed single-chain fragments (scFv) of B7. The scFv may be useful for the **imaging** of myocardial necrosis

after myocarditis, cardiac drug toxicosis or graft rejection. The aim of the authors' work was to **purify** the scFv for immunoscintigraphy. The authors describe several **purification** steps including **immobilized** metal affinity chromatog. (IMAC), anti-c-myc monoclonal antibody affinity chromatog., size-exclusion chromatog. with Superdex 75 HR 10/30 and ion-exchange chromatog. (mini Q TM 30Q).

REFERENCE COUNT: 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L22 ANSWER 13 OF 38 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1999:808079 HCAPLUS

DOCUMENT NUMBER: 132:134319

TITLE: Profiling of amyloid  $\beta$  peptide variants using SELDI protein chip arrays

AUTHOR(S): Davies, Huw; Lomas, Lee; Austen, Brian

CORPORATE SOURCE: CIPHERGEN Biosystems, Surrey, UK

SOURCE: BioTechniques (1999), 27(6), 1258-1261

CODEN: BTNQDO; ISSN: 0736-6205

PUBLISHER: Eaton Publishing Co.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The profile of amyloid  $\beta$  ( $A\beta$ ) peptide variants **secreted** into the media of human cultured **cells** that express the amyloid precursor protein was examined by Surface Enhanced Laser Desorption/Ionization (SELDI) ProteinChip technol. from CIPHERGEN Biosystems using biol. active ProteinChip Arrays. An anti- $A\beta$  polyclonal antibody (anti-NTA4) was used to capture and **purify** multiple immunoreactive  $A\beta$  fragments from a single microliter of media onto the ProteinChip Array. Fragments retained on the surface of the ProteinChip Array were detected directly by mass in the ProteinChip System to provide detailed information on the identity of different  $A\beta$  variants **secreted** from the cultured **cells**. We discuss existing and potential applications of this immunoassay for the detection and relative quantitation of  $A\beta$  species from both cultured **cell** systems and clin. samples.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L22 ANSWER 14 OF 38 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1997:585538 HCAPLUS

DOCUMENT NUMBER: 127:291761

TITLE: Studies of **cell** adhesion and flow cytometric analyses of degranulation, surface phenotype, and viability using human eosinophils, basophils, and mast **cells**

AUTHOR(S): Bochner, Bruce S.; Sterbinsky, Sherry A.; Saini, Sarbjit A.; Columbo, Michele; MacGlashan, Donald W., Jr.

CORPORATE SOURCE: Dep. of Med., Div. of Clin. Immunol., Johns Hopkins Asthma and Allergy Cent., Johns Hopkins Univ. Sch. of Med., Baltimore, MD, 21224, USA

SOURCE: Methods (San Diego) (1997), 13(1), 61-68

CODEN: MTHDE9; ISSN: 1046-2023

PUBLISHER: Academic

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Products derived from eosinophils, basophils, and mast **cells** are considered critical to the development of allergic diseases. Studies of the selective recruitment, accumulation, and/or activation of these **cells** during human allergic inflammatory reactions in vitro and in



vivo have been facilitated by a wide variety of **methods**. Some have been developed to identify and isolate these **cells** from a variety of sites, including blood, airway **secretions**, and surgical or autopsy tissues. Once enriched in purity, assays of **cell** adhesion to endothelium, epithelium, matrix proteins, and **purified, immobilized** counterligands for integrins, selectins, or Ig gene superfamily structures can be performed in vitro under both static and flow conditions. Techniques involving flow cytometry, utilizing characteristics of **cellular light** scatter and immunofluorescence, have permitted the elucidation of **cell** surface phenotype and have aided in quantification of **cellular** degranulation and viability. These approaches have yielded new information on the function of human eosinophils, basophils, and mast **cells** and have suggested unique **cell**-specific pathways of **cell** recruitment, activation, and survival that may contribute to the pathogenesis of allergic diseases.

REFERENCE COUNT: 66 THERE ARE 66 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L22 ANSWER 15 OF 38 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1997:497423 HCAPLUS

DOCUMENT NUMBER: 127:219283

TITLE: Interleukin 12 and B7/CD28 interaction synergistically upregulate interleukin 10 production by human T **cells**

AUTHOR(S): Peng, Xiaohui; Kasran, Ahmad; Ceuppens, Jan L.

CORPORATE SOURCE: Lab. Exp. Immunol., Dep. Pathophysiol., Fac. Med., Catholic Univ. Leuven, Louvain, Belg.

SOURCE: Cytokine (1997), 9(7), 499-506

CODEN: CYTIE9; ISSN: 1043-4666

PUBLISHER: Academic

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Interleukin 12 (IL-12) is a heterodimeric cytokine which promotes the development of Th1 **cells** and their interferon  $\gamma$  (IFN- $\gamma$ ) production after TCR/CD3 triggering. Previous reports indicate that IL-12 synergizes with accessory signalling through B7/CD28 interaction in inducing proliferation and IFN- $\gamma$  production by human T **cells**. In this study, we investigated the capacity of IL-12 to modify cytokine synthesis by freshly **purified** human peripheral blood T **cells** stimulated with anti-CD3 as the primary signal and with CD80 on transfected mouse **cells** as an accessory signal. Our data demonstrate that IL-12 indeed synergizes with B7/CD28 interaction, not only in inducing IFN- $\gamma$  production, but also in enhancing IL-10 synthesis in a dose-dependent manner. In contrast, IL-4 and IL-5 production were **slightly** inhibited by IL-12. The effect of IL-12 on the **secretion** of IL-10 was confirmed by stimulating T **cells** in the absence of accessory **cells** with **immobilized** anti-CD3 mAb and soluble anti-CD28 mAb. CD80 and IL-12 mainly costimulated CD4+CD45RO+ T **cells** but not CD8+ or CD45RA+ T **cells** to produce IL-10. Cyclosporin A (CsA) partially inhibited, and a neutralizing anti-IL-2 mAb in combination with anti-IL-2R mAbs (anti-Tac and Mik $\beta$ 1) strongly reduced IL-10 production. On the other hand, IL-12 did not affect IL-2 production. The data thus suggest a model in which optimal IL-10 production by stimulated peripheral blood T **cells** results from the co-operation of IL-12, B7/CD28 interaction and the ensuring IL-2 activity.

REFERENCE COUNT: 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L22 ANSWER 16 OF 38 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1997:311170 HCAPLUS

DOCUMENT NUMBER: 126:304915

TITLE: A soluble derivative of a mammalian Fc receptor with pH-dependent binding of antibodies

INVENTOR(S): Gastinel, Louis N.; Bjorkman, Pamela J.

PATENT ASSIGNEE(S): California Institute of Technology, USA

SOURCE: U.S., 30 pp., Cont. of U. S. Ser. No. 819,413, abandoned.

CODEN: USXXAM

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5623053	A	19970422	US 1993-4492	19930114 <--
PRIORITY APPLN. INFO.:			US 1992-819413	B1 19920110 <--

AB A soluble Fc receptor derivative (pHsFcR) that shows pH-regulated binding of antibodies is described. The receptor binds antibody in the pH range 5.5-6.5 and releases it in the pH range 7.5-8.5. This analog can still bind the  $\beta$ 2-microglobulin **light** chain to form a fully functional receptor. In particular, the pH-sensitive Fc receptors of neonates are preferred. These derivs. have uses in e.g. the **purification** of antibodies manufactured on a large or small scale. The pHsFcR is a C-terminal truncation derivative lacking the transmembrane domain manufactured by expression of a cDNA for the receptor carrying in-frame stop codons. The pHsFcR is **secreted** into the growth medium upon expression of the cDNA in a suitable (prokaryotic or eukaryotic) host and can be **purified** from the medium by affinity chromatog. against an **immobilized** antibody. A truncation derivs. of the rat intestinal neonatal Fc receptor were prepared using sequence similarities with class I MHC antigens. Expression constructs for analogs carrying the phosphatidyl anchoring signal of decay-accelerating factor were constructed by standard **methods**. Bicistronic constructs carrying the gene for the  $\beta$ 2-microglobulin **light** chain were also constructed. Manufacture of these analogs in CHO **cells** is demonstrated.

L22 ANSWER 17 OF 38 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1997:142648 HCAPLUS

DOCUMENT NUMBER: 126:220774

TITLE: Biophysical and biological properties of naturally occurring high molecular weight insulin-like growth factor II variants

AUTHOR(S): Valenzano, Kenneth J.; Health-Monnig, Ellen;

CORPORATE SOURCE: Tollefsen, Sherida E.; Lake, Mats; Lobel, Peter

SOURCE: Center for Advanced Biotechnology and Medicine and Department of Pharmacology, University of Medicine and Dentistry of New Jersey, Piscataway, NJ, 08854, USA

JOURNAL OF BIOLOGICAL CHEMISTRY (1997), 272(8), 4804-4813.

CODEN: JBCHA3; ISSN: 0021-9258

PUBLISHER: American Society for Biochemistry and Molecular Biology

DOCUMENT TYPE: Journal

LANGUAGE: English

AB A soluble form of the insulin-like growth factor II/mannose 6-phosphate receptor (sIGF-II/MPR) is present in fetal bovine serum and carries mature

7.5-kDa insulin-like growth factor II (IGF-II) and at least 12 different high mol. weight (Mr) IGF-II isoforms (Valenzano, K. J., et al. (1995)). In this study, we used **gel** filtration and anion exchange chromatog. to resolve the isoforms into eight fractions that were characterized with respect to their biochem., biophys., and biol. properties. Each fraction contained one to three major protein species with apparent sizes ranging from 11 to 17 kDa by SDS-polyacrylamide **gel** electrophoresis. The 11-kDa species contains no post-translational modifications and consists of an extended IGF-II backbone terminating at Gly-87. The remaining high Mr IGF-II isoforms are also composed of an 87-amino acid IGF-II peptide backbone but contain increasing amts. of sialated, O-linked sugars. Plasmon resonance spectroscopy expts. revealed that all the high Mr isoforms and mature 7.5-kDa IGF-II bound to **immobilized** recombinant soluble human IGF-I receptor, recombinant human IGF-binding protein 1, and sIGF-II/MPR with similar kinetics. In addition, radiolabeled tracer expts. demonstrated that both mature and high Mr IGF-II isoforms have similar binding profiles in fetal bovine serum and have similar affinities for IGF-II-binding proteins **secreted** from human fibroblasts. Finally the biol. activity of high Mr IGF-II was shown to be similar to or **slightly** better than mature IGF-II in stimulating amino acid uptake in fibroblasts and in inducing myoblast differentiation.

REFERENCE COUNT: 54 THERE ARE 54 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L22 ANSWER 18 OF 38 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1997:122037 HCAPLUS

DOCUMENT NUMBER: 126:210982

TITLE: Modulation of proliferation and lymphokine **secretion** of murine CD4+ T **cells** and cloned Th1 **cells** by proteins of the **extracellular** matrix

AUTHOR(S): Tschoetschel, Ursula; Schwing, Jens; Frosch, Stefanie; Schmitt, Edgar; Schuppan, Detlef; Reske-Kunz, Angelika B.

CORPORATE SOURCE: Inst. Immunology, Johannes Gutenberg-Univ., Mainz, 55101, Germany

SOURCE: International Immunology (1997), 9(1), 147-159

CODEN: INIMEN; ISSN: 0953-8178

PUBLISHER: Oxford University Press

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The authors investigated the co-stimulatory signaling capacity of diverse proteins of the **extracellular** matrix (ECM) for murine resting CD4+ T **cells** and Th1 clone **cells**, activated by **immobilized** anti-CD3 mAb. ECM proteins used in various concns. had no effect on IL-2 production or proliferation of highly **purified** CD4+ T **cell** populations. When the preparation of CD4+ T **cells** contained contaminating accessory **cells**, IL-2 **secretion** and proliferation was enhanced in the presence of co-**immobilized** collagens or fibronectin. However, the level of proliferation attainable by added **irradiated** splenocytes was not reached. Using Th1 **cell** clone M4, enhanced production of IL-2 in the presence of **immobilized** ECM proteins was observed. At a submitogenic anti-CD3 mAb dose, proliferation of M4 T **cells** was augmented by the ECM proteins in a concentration range that optimally induced IL-2 production. IL-2R p55 was up-regulated on M4 T **cells** by collagen type IV and fibronectin to the same level that was induced by exogenously added IL-2, whereas added accessory **cells** induced a higher level of IL-2R p55 expression. Likewise, in dot-blot anal. a

comparable quantity of IL-2R p55- and p75-specific transcripts was induced by collagen type IV or fibronectin and by IL-2, which was lower than that induced by antigen-presenting **cells**. Thus, the enhanced proliferation of M4 T **cells** induced by ECM proteins is not the consequence of direct up-regulation of IL-2R, but appears to be due indirectly to elevated **secretion** of IL-2. At an optimal anti-CD3 mAb dose the collagens inhibited M4 T **cell** proliferation. Diminished **cell** surface expression of IL-2R p55 following stimulation with anti-CD3 mAb plus collagen type IV compared with anti-CD3 mAb alone was observed and may be responsible for growth inhibition.

L22 ANSWER 19 OF 38 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1996:82446 HCAPLUS

DOCUMENT NUMBER: 124:142940

TITLE: Single-chain antibodies. Bacterial production, biosynthetic lipid tagging and use in the preparation of immunoliposomes.

AUTHOR(S): Laukkanen, Marja-Leena

CORPORATE SOURCE: Dep. Biosci., Univ. Helsinki, Helsinki, Finland

SOURCE: VTT Publications (1995), 232, 5-84

CODEN: VTTPEY; ISSN: 1235-0621

PUBLISHER: Valtion Teknillinen Tutkimuskeskus

DOCUMENT TYPE: Journal

LANGUAGE: English

AB A single-chain antibody (Ox scFv) was constructed by combining the variable domains of the heavy and **light** chains of an anti-2-phenyloxazolone IgG via a 28-amino acid residue long natural linker peptide derived from a fungal **cellulase**. The bacterially expressed Ox scFv was correctly processed and **secreted** to the periplasm of Escherichia coli, and after **cell** lysis accumulated into the culture medium. By hapten affinity chromatog. the single-chain antibody was **purified** from the culture medium to essential homogeneity with a yield of 1-2 mg/L. In comparison with the intact parental antibody, the Ox scFv showed similar affinity to **immobilized** hapten but was **slightly** less stable at low pH and high temps. Possibilities for stable **immobilization** of the single-chain antibody to lipid membranes were investigated. To circumvent chemical treatment for constructing a membrane-anchored antibody, the advantage of genetic engineering was utilized and the signal peptide with 9 N-terminal amino acid residues of the major lipoprotein (lpp) of E.coli was fused to the N-terminus of the Ox scFv. This design subjected the antibody fusion protein (Ox lpp-scFv) to an in vivo enzymic addition of a glycerolipid moiety to the N-terminal cysteinyl residue of lpp. The Ox lpp-scFv was expressed in E.coli and, unlike its soluble counterpart, it was firmly associated with the bacterial outer membrane and was metabolically labeled with radioactive palmitate, indicating the biosynthetic lipid-tagging. The lipid-tagged antibody solubilized with nonionic detergents displayed hapten-binding properties comparable to those of the soluble Ox scFv. By removal of the detergent in dialysis the Ox lpp-scFv was incorporated into liposomes with retention of binding activity. To facilitate **purification** by **immobilized** metal affinity chromatog. (IMAC), the C-terminal hexahistidiny tag was engineered into the Ox lpp-scFv. The Ox lpp-scFv-H6 was **purified** by using a 2-step chromatog. procedure with a yield of 0.4-1.6 mg from **cells** harvested from 1 h culture. In the presence of pure phospholipids the **purified** lipid-tagged antibody was efficiently incorporated to liposomes by dialysis. The resulting immunoliposomes with a homogeneous population of 100-2000 nm vesicles showed specific hapten-binding activity. The multivalent binding nature of the immunoliposomes was observed

by the SPR anal. in the BIAcore system. The potential of the biosynthetically lipid-tagged antibody for the functionalization of Eu-chelate loaded liposomes was demonstrated. In comparison with Eu-labeled free single-chain antibody, the immunoliposomal reagent with the higher content of Eu-label produced higher signals and showed better sensitivity. Biosynthetic lipid tagging in *E. coli* is an alternative to present chemical in vitro conjugation for converting the otherwise soluble antibody to membrane-anchored form. The resulting lipid-modified antibody is stoichiometrically labeled at the defined location, and thus it can be **immobilized** into lipid membranes in a stable, oriented, and functional manner.

L22 ANSWER 20 OF 38 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1995:1003449 HCAPLUS

DOCUMENT NUMBER: 124:53062

TITLE: A COS-**cell**-based system for rapid production and quantification of scFv:IgCk antibody fragments

AUTHOR(S): Ridder, Ruediger; Geisse, Sabine; Kleuser, Beate; Kawalleck, Petra; Gram, Hermann

CORPORATE SOURCE: Preclinical Research, Sandoz Pharma Ltd., Basel, CH-4002, Switz.

SOURCE: Gene (1995), 166(2), 273-6

CODEN: GENED6; ISSN: 0378-1119

PUBLISHER: Elsevier

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Single-chain Fv (scFv) antibody (Ab) fragments were transiently produced in COS-1 **cells** utilizing a mammalian expression vector featuring a murine Ig **light**-chain leader sequence for efficient **secretion** and a murine Ig  $\kappa$  constant domain (IgCk) for detection. Several hundred milliliters of supernatants from large-scale COS **cell** transfections were sufficient to **purify** the scFv:IgCk fusion proteins by one-step affinity chromatog. utilizing an **immobilized** rat anti-mouse IgCk monoclonal Ab. Furthermore, the murine IgCk domain allowed for accurate quantification of the scFv:IgCk fusion protein **secreted** into the COS **cell** supernatant by a sandwich ELISA (S-ELISA).

L22 ANSWER 21 OF 38 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1995:901920 HCAPLUS

DOCUMENT NUMBER: 123:312198

TITLE: The induction of human T **cell** unresponsiveness by soluble anti-CD3 mAb requires T **cell** activation

AUTHOR(S): Willems, Fabienne; Andris, Fabienne; Xu, Danlin; Abramowicz, Daniel; Wissing, Martin; Goldman, Michel; Leo, Oberdan

CORPORATE SOURCE: Hopital Erasme, Univ. Libre de Bruxelles, Brussels, B-1070, Belg.

SOURCE: International Immunology (1995), 7(10), 1593-8

CODEN: INIMEN; ISSN: 0953-8178

PUBLISHER: Oxford University Press

DOCUMENT TYPE: Journal

LANGUAGE: English

AB To obtain an in vitro model of human T **cell** unresponsiveness induced by soluble anti-CD3 mAb in the presence of accessory **cells**, T **cells purified** from peripheral blood of healthy volunteers were cultured for 4 days with **irradiated** accessory

**cells** and OKT3. After a 48 h resting period allowing TCR-CD3 complex re-expression, T **cells** were rechallenged with plastic-immobilized OKT3, and their proliferative response as well as their **secretion** of IL-2, IFN- $\gamma$  and IL-10 measured. Primary culture with OKT3 induced a state of unresponsiveness characterized by defective responses to OKT3 rechallenge but normal or enhanced responses to PMA and A23187 calcium ionophore, indicating a defect in the early steps of TCR-CD3-mediated signal transduction. Indeed, the authors found that unresponsive T **cells** displayed an impaired mobilization of **intracellular** calcium stores upon TCR-CD3 ligation. To determine whether the development of unresponsiveness depends on the initial T **cell** activation triggered by OKT3, the authors compared several versions of OKT3 differing in their ability to bind Fc receptors. The authors found that only the activating antibodies that bind Fc receptors on accessory **cells** induced T **cell** unresponsiveness. The authors conclude that human resting T **cells** can be rendered unresponsive by anti-CD3 mAb in soluble form provided that they trigger T **cell** activation.

L22 ANSWER 22 OF 38 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1995:786919 HCAPLUS

DOCUMENT NUMBER: 123:221440

TITLE: Do catalytically active antibodies exist in a healthy human? (Protein kinase activity of sIgA antibodies from human milk)

AUTHOR(S): Kit, Yu.J.; Semenov, D. V.; Nevinsky, G. A.

CORPORATE SOURCE: Novosibirsk Institute of Bioorganic Chemistry, Siberian Branch of Russian Academy of Sciences, Novosibirsk, 630090, Russia

SOURCE: Molekulyarnaya Biologiya (Moscow) (1995), 29(4), 893-906

CODEN: MOBIBO; ISSN: 0026-8984

PUBLISHER: Nauka

DOCUMENT TYPE: Journal

LANGUAGE: Russian

AB The fraction of **secretory** IgA (sIgA) from the milk of healthy mothers was **purified** by sequential affinity chromatog. on protein A-Sepharose (in the presence of 1% Triton X-100), adsorbent Toyopearl HW-55 (**gel-filtration**), DEAE **cellulose** (separation of IgG and IgA antibodies), affinity sorbents with **immobilized** ATP and casein. The protein obtained corresponded to sIgA antibodies according to all known criteria and did not contain any protein contamination. The ability of sIgA to phosphorylate selectively serine residues of casein (not histones) in the presence of [ $\gamma$ -32P]ATP was shown. **Purified** kinase activity was stable at acid shock (pH 2.3), strongly interacted with **immobilized** antibodies against H-chain of sIgA and eluted from the sorbent with the peak corresponding to sIgA antibodies. The complex of sIgA and ATP was stable under the conditions of **gel-filtration**. Affinity modification of sIgA by chemical reactive analogs of ATP resulted in preferential modification of its **light** chain (2-3 mol reagent per mol of dimer form). Under the conditions of oligomer dissociation ATP-Sepharose sorbed only the **light** chains of sIgA. The sIgA have optimal conditions for phosphorylating activity different from those of known protein kinases. We suppose that sIgA antibodies with kinase activity are a first example of sIgA antibodies with catalytic activity. For the first time the possibility of existence of natural abzymes in a healthy human was shown. These abzymes catalyze the reaction of synthesis but not substrate degradation reaction.

L22 ANSWER 23 OF 38 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1995:719644 HCAPLUS  
DOCUMENT NUMBER: 123:139785  
TITLE: Spermatocytes and round spermatids of rat testis:  
protein patterns  
AUTHOR(S): Cossio, Gabriela; Sanchez, Jean-Charles; Golaz,  
Olivier; Wettstein, Rodolfo; Hochstrasser, Denis F.  
CORPORATE SOURCE: Div. Biol. Molecular, Inst. Investigaciones Biol.  
"Clemente Estable", Montevideo, Urug.  
SOURCE: Electrophoresis (1995), 16(7), 1225-30  
CODEN: ELCTDN; ISSN: 0173-0835  
PUBLISHER: VCH  
DOCUMENT TYPE: Journal  
LANGUAGE: English

AB Spermatogenesis is a process in the testis that involves meiotic **cell** division and spermiogenesis. The mechanisms of regulation and its associated proteins are mostly unknown. This publication shows the two-dimensional (2-D) **gel** electrophoresis protein map obtained from rat testis using nonlinear 3.5-10 **immobilized** pH gradients for the first-dimensional separation. Eighteen proteins were successfully identified in the SWISS-PROT protein database using amino acid anal. of proteins recovered from polyvinylidene difluoride (PVDF) membranes and verified for one of them by comparison with Anderson's rat liver reference map. Fourteen new polypeptides were identified and four were previously known. Two of these new proteins were closely related to the spermatogenetic process. T-complex protein 1 is expressed in large amts. in germ **cells**. Androgen-dependent sperm-coating glycoprotein is **secreted** by epididymal **cells**. In order to detect changes in protein expression during meiosis and spermiogenesis, spermatocytes and round spermatid **cell** populations were **purified** by centrifugal elutriation and compared. In this way several proteins not found in the spermatocyte 2-D **images** could be high-**lighted**. The sperm-coating glycoprotein was thus shown to be present in large amts. in round spermatids.

L22 ANSWER 24 OF 38 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1995:559397 HCAPLUS  
DOCUMENT NUMBER: 122:312695  
TITLE: T **cell**-induced B **cell** blasts  
differentiate into plasma **cells** when  
cultured on bone marrow stroma with IL-3 and IL-10  
AUTHOR(S): Merville, Pierre; Dechanet, Julie; Grouard, Geraldine;  
Durand, Isabelle; Banchereau, Jacques  
CORPORATE SOURCE: Schering-Plough/Lab. Immunol. Res., Dardilly, 69 571,  
Fr.  
SOURCE: International Immunology (1995), 7(4),  
635-43  
CODEN: INIMEN; ISSN: 0953-8178  
PUBLISHER: Oxford University Press  
DOCUMENT TYPE: Journal  
LANGUAGE: English

AB B lymphocytes activated by T **cells** in secondary lymphoid organs mature into plasma **cells** after migration into the medullary cords of these organs, mucosal lamina propria or bone marrow. To analyze each step leading to plasma **cell** generation, the authors set up a two-step culture system of **purified** tonsillar B **cells**. In a primary stage, B **cell** blasts were generated by co-culturing B **cells** with an **irradiated** T **cell** clone activated with **immobilized** anti-CD3. In a secondary step, culturing these blasts on bone marrow stromal **cells** (BMSC)

induced them to **secrete** large amts. of IgG, as well as some IgM and IgA. Other fibroblast-like **cell** lines were less efficient at sustaining the differentiation of blasts into Ig-secreting **cells**, suggesting that these are specific properties of BMSC. Addition of IL-3 and IL-10 further stimulated IgG **secretion** by B **cell** blasts cultured on BMSC, mostly the IgG1 subclass. These two cytokines probably acted through different pathways, as (i) the effect of IL-3 but not IL-10 was dependent upon prolonged T **cell** pre-activation and (ii) their combined stimulatory effect was additive. B **cell** blasts cultured on BMSC with a combination of IL-3 and IL-10 differentiated into non-proliferating plasma **cells** as determined by poor thymidine incorporation, typical **cellular** morphol., intense expression of intracytoplasmic Igs, very high levels of surface CD38 and lack of surface CD20.

L22 ANSWER 25 OF 38 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1995:476747 HCAPLUS

DOCUMENT NUMBER: 122:262003

TITLE: Fibronectin and 130-kDa molecule complex mimics snake venom botrocetin-like structure potentially modulating association between von Willebrand factor and vascular vessel wall

AUTHOR(S): Katayama, Masahiko; Nagata, Satomi; Hirai, Sayuri; Miura, Shuji; Fujimura, Yoshihiro; Matusi, Taei; Kato, Ikunoshin; Titani, Koiti

CORPORATE SOURCE: Takara Shuzo Co., Ltd., Biotechnology Research Labs., Shiga, 520-21, Japan

SOURCE: Journal of Biochemistry (Tokyo) (1995), 117(2), 331-8

CODEN: JOBIAO; ISSN: 0021-924X

PUBLISHER: Japanese Biochemical Society

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The authors established seven hybridomas **secreting** monoclonal antibodies (MoAbs) against the venom from Bothrops jararaca. Six of them were demonstrated to specifically recognize botrocetin, a venom protein which binds with von Willebrand factor (vWf) and induces platelet agglutination. Two of them, BCT4-3 and BCT115-2 MoAbs, could significantly inhibit botrocetin binding with plasma vWf. BCT4-3 could react **slightly** with a monolayer of human endothelial **cells** (ECs), and BCT4-3 binding to ECs was drastically enhanced by the coexistence of human plasma in a dose-dependent manner, indicating that a biol. modulator structurally resembling botrocetin is created initially on the EC surface complexed with some plasma proteins. Botrocetin-like components could be **immunopurified** only by **immobilized** BCT4-3, but not by the other **immobilized** MoAbs, from umbilical vein exts. Interestingly, the immunoisolated materials were identified to consist essentially of fibronectin (Fn) and a 130 kDa mol., and this complex bound to vWf in the exts. Depletion of Fn from plasma decreased BCT4-3 binding to ECs. The epitope of BCT4-3 expressed on the endothelial surface, comprising plasma Fn and the coisolated 130 kDa mol., is proposed to be a physiol. modulator structurally mimicking botrocetin, and essentially supporting vWf-binding to injured endothelium and subsequently to circulating platelets.

L22 ANSWER 26 OF 38 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1994:189670 HCAPLUS

DOCUMENT NUMBER: 120:189670

TITLE: Role of CD40 antigen and interleukin-2 in T **cell**-dependent human B lymphocyte growth



AUTHOR(S): Blanchard, Dominique; Gaillard, Claude; Hermann, Patrice; Banchereau, Jacques  
CORPORATE SOURCE: Lab. Immunol. Res., Schering-Plough, Dardilly, F-69571, Fr.  
SOURCE: European Journal of Immunology (1994), 24(2), 330-5  
CODEN: EJIMAF; ISSN: 0014-2980  
DOCUMENT TYPE: Journal  
LANGUAGE: English

AB In the present study, the authors examined the participation of CD40 ligand (L)-CD40 interaction in T **cell**-dependent B **cell** responses. To this end, **purified** B lymphocytes were cultured over **irradiated** CD4+ cloned T **cells** activated with **immobilized** anti-CD3 antibody. The anti-CD40 mAb 89 strongly blocked, in a specific fashion, both proliferation and Ig **secretion** of tonsil B **cells**. Interestingly, proliferation of surface (s)IgD+ B **cell** was less inhibited by anti-CD40 than that of sIgD- **cells**. Preactivated T **cells** induced B **cells** to grow and **secrete** Igs preferentially in response to IL-2. This contrasts with the CD40 system where B **cells** are essentially responsive to IL-4 and IL-10 but not to IL-2 alone. Collectively, these data indicate that CD40L-CD40 interaction plays an important role in IL-2-mediated T **cell**-dependent B **cell** responses. However, the activation of a subset of sIgD+ **cells** may be independent of this interaction.

L22 ANSWER 27 OF 38 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1994:189378 HCAPLUS  
DOCUMENT NUMBER: 120:189378  
TITLE: Role of opioid peptides in the regulation of cytokine production by murine CD4+ T **cells**  
AUTHOR(S): van den Bergh, Paula; Dobber, Ruud; Ramlal, Sharmila; Rozing, Jan; Nagelkerken, Lex  
CORPORATE SOURCE: Inst. Ageing Vasc. Res., TNO, Leiden, 2300 AK, Neth.  
SOURCE: Cellular Immunology (1994), 154(1), 109-22  
CODEN: CLIMB8; ISSN: 0008-8749  
DOCUMENT TYPE: Journal  
LANGUAGE: English

AB The presence of the opioid peptides  $\alpha$ - and  $\beta$ -endorphin (-End) but not methionine enkephalin (Met-enk) in in vitro cultures of **purified** CD4+ T **cells**, stimulated with Con A in the presence of **irradiated** spleen **cells**, resulted in a threefold stimulation of IL-2, IL-4, and IFN- $\gamma$  production. The stimulating effect was dependent on the concentration of the peptides and reached optimal values in the dose range from  $10^{-12}$  to  $10^{-10}$  M. Similar results were obtained when **purified** CD4+ T **cells** were stimulated with **immobilized** anti-CD3, indicating a direct effect of opioid peptides on CD4+ T **cells**. Moreover, in this system a twofold enhancement of IL-6, but not IL-1, **secretion** was observed. These stimulatory effects were not mediated through opioid receptors since the peptide fragment  $\beta$ -End6-31 that lacks the N-terminal opioid receptor binding part was still stimulatory. This is in agreement with the finding that  $\beta$ -End did not affect cAMP, is described for the triggering of classical opioid receptors. Expts. undertaken to reveal the mechanism of action of opioid peptides suggest an overall enhancement of lymphokine production: (1) enhancement of IL-4 production occurred also in the presence of excess IL-2; and (2) neither IL-1 receptor-antagonizing protein nor anti-IL-6 were able to abrogate the stimulatory effect on IL-2 and IL-4 production. Finally, the presence and activity of opioid receptors in

cultures of CD4+ T **cells** were substantiated by the fact that the opioid receptor antagonist naloxone by itself enhanced cytokine synthesis, which points to the endogenous production by lymphocytes of down-regulating opioid peptides.

L22 ANSWER 28 OF 38 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1994:189371 HCAPLUS

DOCUMENT NUMBER: 120:189371

TITLE: Differential effects of interleukin-12 on the development of naive mouse CD4+ T **cells**

AUTHOR(S): Schmitt, Edgar; Hoehn, Petra; Germann, Tieno; Ruede, Erwin

CORPORATE SOURCE: Inst. Immunol., Mainz, D-55101, Germany

SOURCE: European Journal of Immunology (1994), 24(2), 343-7

CODEN: EJIMAF; ISSN: 0014-2980

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The influence of interleukin (IL)-12 and IL-4 on the differentiation of naive CD4+ T **cells** was studied in an accessory **cell**-free in vitro system. Dense CD4+ T **cells** were **purified** from unimmunized mice and activated using **immobilized** anti-CD3 monoclonal antibodies (mAb) in the presence of IL-4, IL-12, or a combination of both cytokines, and restimulated after 6 days by re-exposure to anti-CD3-coated culture wells. T **cells** initially activated in the presence of IL-4 produced substantial amts. of IL-4 and trace amts. of interferon (IFN)- $\gamma$  after restimulation at day 6 with plate-bound anti-CD3 mAb. By contrast, T **cells** primed in the presence of IL-12 produced high levels of IFN- $\gamma$  and only minimal amts. of IL-4, thus indicating that IL-2 and IL-4 by acting directly on stimulated naive CD4+ T **cells** support the development of TH1 and TH2 **cells**, resp. When naive CD4+ T **cells** were stimulated in the presence of IL-12 together with IL-4 in comparable concns., the effect of IL-12 on TH1 differentiation was largely inhibited by IL-4. IL-12 exerted no inhibitory effect on IL-4-induced TH2 differentiation but rather enhanced the production of IL-4 after restimulation of the resp. T **cells**. Decreasing amts. of IL-4 in combination with a high level of IL-12 led to an increasing production of IFN- $\gamma$  by the emerging T **cells** and, simultaneously, to a relatively high production of IL-4. These data were confirmed by time-course expts. which revealed that the delayed addition of IL-4 to IL-12-primed T **cell** cultures resulted in a gradual restoration of IFN- $\gamma$  production whereas in parallel the **secretion** of IL-4 was not reduced over a wide period of delay (6-72 h). These results, therefore, demonstrate that (a) IL-4 dominates the effect of IL-12, (b) IL-12 promotes the development of TH1 **cells**; however, in the presence of IL-12 and relatively high levels of IL-4 also the development of TH2-like **cells** is **slightly** enhanced by IL-12, and (c) high amts. of IL-12 in combination with relatively low levels of IL-4 give rise to a T **cell** population that upon rechallenge exhibited a cytokine profile resembling that of TH0 **cells**.

L22 ANSWER 29 OF 38 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1994:98963 HCAPLUS

DOCUMENT NUMBER: 120:98963

TITLE: Antagonism of the **intracellular** action of botulinum neurotoxin type A with monoclonal antibodies that map to **light-chain** epitopes

AUTHOR(S): Cenci di Bello, Isabelle; Poulain, Bernard; Shone, Clifford C.; Tauc, Ladislav; Dolly, J. Oliver

CORPORATE SOURCE: Dep. Biochem, Imp. Coll. Sci., Technol Med., London, UK

SOURCE: European Journal of Biochemistry (1994), 219(1-2), 161-9  
CODEN: EJBCAI; ISSN: 0014-2956

DOCUMENT TYPE: Journal

LANGUAGE: English

AB MAb's were produced in mice against highly **purified**, renatured **light** chain (LC) of botulinum neurotoxin A (BoNT A) that was **immobilized** on **nitrocellulose** to avoid the undesirable use of toxoids. S.c. implants of relatively high amts. (up to 10 µg each) of LC allowed its slow release into the systemic circulation, and, thus, yielded much higher antibody titers against the underivatized antigen than had hitherto been obtained by conventional immunization. Seven stable hybridoma **cell** lines were established which **secrete** mAb of IgG1 and IgG2b subclasses and reacted specifically with BoNT A and LC, in native and denatured states, without showing any cross-reactivity with types B, E, F, or tetanus toxin. The pronounced reactivities of 3 mAbs towards refolded LC or intact toxin, observed in immunobinding and precipitation assays, relative to that in Western blots imply a preference for conformational epitopes. Though mAbs 4, 5, and 7 failed to neutralize the lethality of BoNT in vivo, administration intraneurally of mAb7 prevented the inhibition of transmitter release normally induced by subsequent **extracellular** administration of BoNT A. Notably, the latter mAb reacted with a synthetic peptide corresponding to amino acids 28-53 in the N-terminus of the LC, a highly conserved region in Clostridial neurotoxins reported to be essential for maintaining the tertiary structure of the chain. Most importantly, when mAbs 4 or 7 were microinjected inside ganglionic neurons of Aplysia, each totally reversed, though transiently, the blockade of acetylcholine release by the toxin; this novel finding is described in relation to the nature of zinc-dependent protease activity of the toxin.

L22 ANSWER 30 OF 38 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1993:426328 HCAPLUS

DOCUMENT NUMBER: 119:26328

TITLE: Characterization of humanized anti-p185HER2 antibody Fab fragments produced in Escherichia coli

AUTHOR(S): Kelley, R. F.; O'Connell, M. P.; Carter, P.; Presta, L.; Eigenbrot, C.; Covarrubias, M.; Snedecor, B.; Speckart, R.; Blank, G.; et al.

CORPORATE SOURCE: Anal. Chem. Dep., Genentech, Inc., South San Francisco, CA, 94080, USA

SOURCE: ACS Symposium Series (1993), 526(Protein Folding), 218-39  
CODEN: ACSMC8; ISSN: 0097-6156

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The authors have been using biochem. and biophys. **methods** to characterize chimeric and humanized variants of the murine monoclonal antibody 4D5, directed against human epidermal growth factor receptor 2 (p185HER2). These studies were performed on antibody Fab fragments produced by **secretion** from E. coli. Humanized Fab fragment (hu4D5-8 Fab) was expressed at very high levels (1-2 g/L), whereas chimeric Fab (ch4D5 Fab) was expressed at much lower titers (5-20 mg/L), as determined by antigen-binding ELISA of supernatants from 10 L ferms. Hu4D5-8 Fab and ch4D5 Fab **purified** by using affinity chromatog. on **immobilized** bacterial IgG-binding proteins gave identical far UV-CD spectra characteristic of the Ig fold. Thermodyn. studies of antigen

binding show comparable affinities ( $\Delta G$ ) for ch and hu4D5-8 Fab, but different  $\Delta H$  values suggesting **slight** differences in the mechanism of binding. This difference is reflected in the anti-proliferative activity of these fragments on human breast tumor **cells**.

L22 ANSWER 31 OF 38 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1992:443882 HCAPLUS

DOCUMENT NUMBER: 117:43882

TITLE: Analysis of recombinant proteins by isoelectric focusing in **immobilized** pH gradients

AUTHOR(S): Bischoff, Rainer; Roecklin, Dominique; Roitsch, Carolyn

CORPORATE SOURCE: Protein Anal. Unit, Transgene S. A., Strasbourg, F-67082, Fr.

SOURCE: Electrophoresis (1992), 13(4), 214-19

CODEN: ELCTDN; ISSN: 0173-0835

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Isoelec. focusing in **immobilized** pH gradients (IEF-IPG) was used to analyze three different recombinant proteins. Recombinant leech hirudin (65 amino acids, three disulfide bonds) expressed in *Saccharomyces cerevisiae* as a **secreted** protein and **purified** by anion-exchange and reversed-phase chromatog. proved to be homogeneous with regard to its isoelec. point (pI). In addition, the theor. pI, calculated on the

basis of the primary structure, corresponded precisely to the measured pI of 4.30. IEF-IPG was further employed to follow the stability of recombinant hirudin at pH 9, indicating that deamidation occurred under these conditions. A variant of recombinant human  $\alpha$ 1-antitrypsin (AAT) (389 amino acids, one cysteine residue) expressed in *Escherichia coli* and **purified** by anion-exchange, metal chelate and hydrophobic-interaction chromatog. appeared to be homogeneous by polyacrylamide gel electrophoresis under reducing and denaturing conditions as well as by various high performance liquid chromatog. **methods**. However, some heterogeneity was detected by IEF-IPG between pH 5-6. The measured pI values of 5.43-5.58 were **slightly** lower than the calculated pI based on the primary structure (5.72). This indicated deamidations of Asn or Gln residues. A recombinant *Schistosoma mansoni* parasite antigen, p28 (210 amino acids, one cysteine residue) obtained after **intracellular** expression in *Saccharomyces cerevisiae* and affinity **purification** on glutathione agarose was analyzed by IEF-IPG in a pH 7.3-8.3 gradient. It appeared to be heterogeneous with regard to its pI, with the major component having a pI of 7.81 compared to the calculated value of 7.17. N-Terminal amino acid sequencing as well as amino acid composition anal. were performed on the

separated

forms of p28 after electroblotting showing the feasibility of combining IEF-IPG with subsequent anal. **methods** to obtain structural information.

L22 ANSWER 32 OF 38 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1992:148983 HCAPLUS

DOCUMENT NUMBER: 116:148983

TITLE: Deletion analysis of recombinant human factor V. Evidence for a phosphatidylserine binding site in the second C-type domain

AUTHOR(S): Ortel, Thomas L.; Devore-Carter, Denise; Quinn-Allen, Mary Ann; Kane, William H.

CORPORATE SOURCE: Med. Cent., Duke Univ., Durham, NC, 27710, USA

SOURCE: Journal of Biological Chemistry (1992),  
267(6), 4189-98  
CODEN: JBCHA3; ISSN: 0021-9258

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The authors have constructed a series of recombinant deletion mutants lacking domain-size fragments of the **light** chain of human factor V (rHFV). These mutants are expressed and **secreted** as single-chain proteins by COS **cells**. Thrombin and the factor V activator from Russell's viper venom process these deletion mutants as expected. The **light** chain deletion mutants possess essentially no procoagulant activity, nor are they activated by treatment with factor V activator from Russell's viper venom. Deletion of the 2nd C-type domain results in essentially complete loss of phosphatidylserine-specific binding, whereas the presence of the C2 domain alone (rHFV des-A3C1, which lacks the A3 and C1 domains of the **light** chain) results in significant phosphatidylserine-specific binding. The presence of the A3 domain alone (rHFV des-C1C2) does not mediate binding to **immobilized** phosphatidylserine. Increasing Ca<sup>2+</sup> concns. result in decreased binding of recombinant human factor V and the mutant rHFV des-A3C1 to phosphatidylserine, similar to previous studies with **purified** plasma factor V and phospholipid vesicles. These results indicate that human factor V, similar to human factor VIII, possesses a phosphatidylserine-specific binding site within the C2 domain of the **light** chain.

L22 ANSWER 33 OF 38 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1992:126478 HCAPLUS

DOCUMENT NUMBER: 116:126478

TITLE: Characterization of a recombinant single-chain molecule comprising the variable domains of a monoclonal antibody specific for human fibrin fragment D-dimer

AUTHOR(S): Laroche, Yves; Demeyer, Marc; Stassen, Jean Marie; Gansemans, Yannick; Demarsin, Eddy; Matthyssens, Gaston; Collen, Desire; Holvoet, Paul

CORPORATE SOURCE: Corvas Int. NV, Ghent, Belg.

SOURCE: Journal of Biological Chemistry (1991),  
266(25), 16343-9  
CODEN: JBCHA3; ISSN: 0021-9258

DOCUMENT TYPE: Journal

LANGUAGE: English

AB A recombinant single-chain mol., scFv-K12G0, containing the variable domains of the monoclonal antibody MA-15C5, specific for fragment D-dimer of human cross-linked fibrin, was constructed and expressed in *Spodoptera frugiperda*, Sf9, insect **cells**. The Arg108 C-terminal amino acid of the variable domain of the **light**-chain of the antibody was connected through a synthetic Ala-Gly-Gln-GLy-Ser-Ser-Val peptide linker with the Gln1 N-terminal amino acid of the variable domain of its heavy chain. ScFv-K12G0 was **secreted** by the infected Sf9 **cells** at a rate of 10 µg/10<sup>6</sup> **cells** within 48 h, resulting in conditioned medium with a maximum concentration of 15 mg of scFv-K12G0/L. The mol., **purified** to homogeneity by ion exchange chromatog. and **gel** filtration, migrated as a single Mr band on reduced SDS-**gel** electrophoresis. It bound to **immobilized** fragment D-dimer with an affinity constant of 4.0 + 10<sup>9</sup> M<sup>-1</sup> (2.0 + 10<sup>10</sup> M<sup>-1</sup> for intact MA-15C5). Clearing of scFv-K12G0 from the circulation in rabbits occurred with an initial half-life (t<sub>1/2α</sub>) of 10 min and a clearance of 5.1 mL min<sup>-1</sup>, as compared to 90 min and 210 mL min<sup>-1</sup> for intact MA-15C5. Nephrectomy

resulted in a prolongation of  $t_{1/2\alpha}$  to 110 min, suggesting that the rapid clearance of scFv-K12G0 occurs primarily via the kidney, presumably by glomerular filtration. Thus, the single-chain recombinant mol. scFv-K12G0 is **secreted** in functionally intact form and it may be useful for targeting of radioisotopes or plasminogen activators to blood clots in vivo.

L22 ANSWER 34 OF 38 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1989:437819 HCAPLUS  
DOCUMENT NUMBER: 111:37819  
TITLE: **Method** for selection of antiidiotype antibodies containing the internal **image** of a pathogen antigen  
INVENTOR(S): Anderson, Darrel R.  
PATENT ASSIGNEE(S): Synbiotics Corp., USA  
SOURCE: Eur. Pat. Appl., 7 pp.  
CODEN: EPXXDW  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 286405	A2	19881012	EP 1988-303109	19880407 <--
EP 286405	A3	19890809		
R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE				
AU 8814361	A1	19881013	AU 1988-14361	19880407 <--
JP 01124381	A2	19890517	JP 1988-85481	19880408 <--
PRIORITY APPLN. INFO.:			US 1987-36027	A 19870408 <--

AB A **method** of selecting an antiidiotype-antibody-producing **cell** having an internal **image** for an antigen of a pathogen comprises (a) incubating a collection of antibody-producing immune **cells** or hybridomas, activated with an affinity-**purified** antiserum specific for the pathogen, with a labeled selective affinity-**purified** antiserum specific for the pathogen; and (b) selecting antibody-producing **cells** that bind the labeled antiserum. Hybridomas producing antibody to heart worm antibody D.I. 130.1 were screened with a dog antiheartworm antiserum, **purified** on a chromatog. column containing **immobilized** heartworm antigens. Of 324 hybridomas, only 39 were found to be **secreting** internal **image** antiidotypic antibodies.

L22 ANSWER 35 OF 38 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1987:631749 HCAPLUS  
DOCUMENT NUMBER: 107:231749  
TITLE: Identification of a 64 kDa heparan sulfate proteoglycan core protein from human lung fibroblast plasma membranes with a monoclonal antibody  
AUTHOR(S): De Boeck, Hilde; Lories, Veerle; David, Guido; Cassiman, Jean Jacques; Van den Berghe, Herman  
CORPORATE SOURCE: Cent. Hum. Genet., Univ. Leuven, Louvain, B-3000, Belg.  
SOURCE: Biochemical Journal (1987), 247(3), 765-71  
CODEN: BIJOAK; ISSN: 0306-3275  
DOCUMENT TYPE: Journal  
LANGUAGE: English

AB Human lung fibroblasts produce heparan sulfate proteoglycans (HSPG) that are associated with the plasma membrane. A monoclonal-antibody (Mab)-**secreting** hybridoma, S1, was produced by fusion of SP 2/0-AG 14

mouse myeloma **cells** with spleen **cells** from mice immunized with partially **purified cellular** HSPG fractions. The HSPG character of the material carrying the epitope recognized by Mab S1 was demonstrated by: (1) the **copurifn.** of the S1 epitope with the membrane HSPG of human lung fibroblasts; (2) the decrease in size of the material carrying the S1 epitope upon treatment with heparinase or heparitinase, and the resistance of this material to heparinase treatment after N-desulfation. The S1 epitope appears to be part of the core protein, since it was **destroyed** by proteinase treatment and by disulfide-bond reduction, but not by treatments that depolymerize the glycosaminoglycan chains and N-linked oligosaccharide chains. PAGE of nonreduced heparitinase-digested membrane HSPG followed by Western blotting and immunostaining with Mab S1 revealed a single band with apparent mol. mass of 65 kDa (kilodaltons). Membrane proteoglycans isolated from detergent exts. or from 4M guanidinium chloride exts. of the **cells** yielded similar results. Addnl. digestion with N-glycanase lowered the apparent mol. mass of the immunoreactive material to 56 kDa, suggesting that the core protein also carries N-linked oligosaccharides. Fractionation of 125I-labeled membrane HSPG by immunoaffinity chromatog. on **immobilized** Mab S1, followed by heparitinase digestion and PAGE of the bound material, yielded a single labeled band with apparent mol. mass 64 kDa. Treatment with dithiothreitol caused a **slight** increase in apparent mol. mass, suggesting that the core protein of this membrane proteoglycan consists of a single subunit containing (an) intrachain disulfide bond(s).

L22 ANSWER 36 OF 38 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1986:623340 HCAPLUS

DOCUMENT NUMBER: 105:223340

TITLE: Calmodulin-binding proteins and calmodulin-regulated enzymes in dog pancreas

AUTHOR(S): Bartelt, Diana C.; Wolff, Donald J.; Scheele, George A.

CORPORATE SOURCE: Lab. Cell Mol. Biol., Rockefeller Univ., New York, NY, 10021, USA

SOURCE: Biochemical Journal (1986), 240(3), 753-63

CODEN: BIJOAK; ISSN: 0306-3275

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Calmodulin (I) was isolated and **purified** to homogeneity from dog pancreas. Highly **purified subcellular** fractions were prepared by zonal sucrose-d. ultracentrifugation and assayed for their ability to bind 125I-labeled (125I-) I in vitro. Proteins contained in these fractions were also examined for binding of 125I-I after their separation by PAGE in SDS. I-binding proteins were detected in all **subcellular** fractions except the zymogen granule and zymogen granule membrane fractions. One I-binding protein (apparent mol.weight (Mr) 240,000), observed in a washed smooth microsomal fraction, had properties similar to those of  $\alpha$ -fodrin. The postribosomal supernatant fraction contained 3 prominent I-binding proteins, with Mrs of 62,000, 50,000, and 40,000. I-binding proteins, prepared from a postmicrosomal supernatant fraction by Ca<sup>2+</sup>-dependent affinity chromatog. on **immobilized** I, exhibited I-dependent phosphodiesterase, protein phosphatase, and protein kinase activities. In the presence of Ca<sup>2+</sup> and I, phosphorylation of smooth muscle myosin **light** chain and brain synapsin and autophosphorylation of a 50,000-Mr protein were observed. Anal. of the protein composition of the preparation by SDS/PAGE revealed a major protein

of Mr 50,000 which bound 125I-I. This protein shares characteristics with the I-dependent multifunctional protein kinase (kinase II) recently observed

to have a widespread distribution. The possible role of I-binding proteins and I-regulated enzymes in the regulation of exocrine pancreatic protein synthesis and **secretion** is discussed.

L22 ANSWER 37 OF 38 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1986:607327 HCAPLUS

DOCUMENT NUMBER: 105:207327

TITLE: **Purification** and properties of a monoclonal antibody specific to the free  $\beta$ -subunit of human chorionic gonadotropin (hCG $\beta$ ) and its use in the isolation of free hCG $\beta$  produced by choriocarcinoma **cells**

AUTHOR(S): Thotakura, Nageswara Rao; Bahl, Om P.

CORPORATE SOURCE: Dep. Biol. Sci., State Univ. New York, Buffalo, NY, 14260, USA

SOURCE: Endocrinology (1986), 119(5), 1887-94

CODEN: ENDOAO; ISSN: 0013-7227

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The free  $\beta$ -subunit of hCG is **secreted** by several tumors and is reported to be different from native hCG $\beta$ . A monoclonal antibody, B158, specific for free hCG $\beta$  was developed to facilitate the detection and isolation of tumor-derived free hCG $\beta$  in the presence of intact hCG and hCG $\alpha$ . B158 belongs to the IgG1 subclass, has high affinity for hCG $\beta$  (affinity constant  $1.05 \times 10^9$  M $^{-1}$ ), and can be obtained in large quantities. The sensitivity of this antibody to detect free hCG $\beta$  in a RIA is  $<1$  ng. B158 has negligible cross-reactivity with hCG, human LH, and other intact glycoprotein hormones and reacts with the free  $\beta$  subunits of deglycosylated hCG, human LH, and ovine LH. The antibody completely inhibits the recombination of hCG $\beta$  with hCG $\alpha$  indicating the antigenic site to be in the subunit interaction region or its vicinity. Comparison of the amino acid sequences of the various cross-reacting and noncross-reacting hormones indicates that the antigenic site may be discontinuous and conformational. B158 was **purified** to homogeneity from ascites fluid by DEAE-Affi-Gel blue and hCG $\beta$  affinity chromatog. **Immobilized** pure B158 antibody was used to isolate free hCG $\beta$  in a homogeneous form and high yield from BeWo choriocarcinoma **cell** culture supernatants. This free hCG $\beta$  has a **slightly** higher mol. weight than standard hCG $\beta$  and recombines normally with hCG $\alpha$ . BeWo **cells** appear to produce only 1 species of free hCG $\beta$ .

L22 ANSWER 38 OF 38 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1982:140899 HCAPLUS

DOCUMENT NUMBER: 96:140899

TITLE: Studies on mouse hybridomas **secreting** IgM or IgA antibodies to  $\alpha(1 \rightarrow 6)$ -linked dextran

AUTHOR(S): Sharon, Jacqueline; Kabat, Elvin A.; Morrison, Sherie L.

CORPORATE SOURCE: Dep. Microbiol., Columbia Univ., New York, NY, 10032, USA

SOURCE: Molecular Immunology (1981), 18(9), 831-46

CODEN: MOIMD5; ISSN: 0161-5890

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Twelve mouse hybridomas **secreting** antibodies to dextran B512, identified by replica immunoadsorption screening of 100,000 **immobilized** hybridoma clones, were obtained. Among 11 hybridomas of BALB/c origin, 7 produced IgM and 4 produced IgA. One hybridoma of C57BL/6 origin formed IgA. A  $\kappa$  **light** chain was



synthesized by each of the 12 hybridomas in addition to the nonspecific  $\kappa$  **light** chain of the parent myeloma. The heavy chain was shown to associate preferentially with the specific (spleen **cell**-derived) **light** chain. All hybridoma antibodies were **purified** from ascites by precipitation with dextran B512, followed by subsequent digestion of the dextran with dextranase. Although all the specific **light** chains migrated identically in SDS **gels** under reducing conditions, variations in migration were noticed among the heavy chains. Differences in migration among the IgA monomers and among the IgA polymers were seen on nondenaturing polyacrylamide **gels**. Densitometer scans of such **gels** showed that >50% of the IgA hybridoma antibodies were in polymeric form. Implications of the preferential association of heavy chain with specific **light** chain, and of the size differences among the heavy chains for the generation of antibody specificity and diversity are discussed.

SEARCH IN MEDLINE, BIOSIS, EMBASE, JAPIO, JICST, WPID

=> d que stat 120

```

L7      255033 SEA FILE=HCAPLUS ABB=ON  ?CELL? AND ?PURIF?
L8      5930 SEA FILE=HCAPLUS ABB=ON  L7 AND ?IMMOBILIZ?
L9      5930 SEA FILE=HCAPLUS ABB=ON  L8 AND (?IMMOBILIZ? OR ?DESTROY? OR
      ?KILL?)
L10     359 SEA FILE=HCAPLUS ABB=ON  L9 AND ?SECRET?
L11     43 SEA FILE=HCAPLUS ABB=ON  L10 AND (?IMAG? OR ?RADIAT? OR
      ?LIGHT?)
L12     10 SEA FILE=HCAPLUS ABB=ON  L11 AND ?METHOD?
L13     43 SEA FILE=HCAPLUS ABB=ON  L11 OR L12
L15     155 SEA L13
L16     98 DUP REMOV L15 (57 DUPLICATES REMOVED)
L17     55 SEA L16 AND ?METHOD?
L20     19 SEA L17 AND GEL?

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=> d ibib abs 120 1-19

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L20 ANSWER 1 OF 19      MEDLINE on STN
ACCESSION NUMBER:      2003427011      MEDLINE
DOCUMENT NUMBER:      PubMed ID: 12968287
TITLE:                Large-scale transient transfection of serum-free
                        suspension-growing HEK293 EBNA1 cells: peptone
                        additives improve cell growth and transfection
                        efficiency.
AUTHOR:                Pham Phuong Lan; Perret Sylvie; Doan Huyen Chau; Cass
                        Brian; St-Laurent Gilles; Kamen Amine; Durocher Yves
CORPORATE SOURCE:      Animal Cell Technology Group, Bioprocess Platform,
                        Biotechnology Research Institute, National Research Council
                        Canada, 6100 Royalmount Avenue, Montreal, Canada H4P 2R2.
SOURCE:                Biotechnology and bioengineering, (2003 Nov 5) Vol. 84, No.
                        3, pp. 332-42.
                        Journal code: 7502021. ISSN: 0006-3592.
PUB. COUNTRY:          United States
DOCUMENT TYPE:          (EVALUATION STUDIES)
                        Journal; Article; (JOURNAL ARTICLE)
                        (VALIDATION STUDIES)
LANGUAGE:              English
FILE SEGMENT:          Priority Journals
ENTRY MONTH:           200405
ENTRY DATE:            Entered STN: 12 Sep 2003
                        Last Updated on STN: 22 May 2004
                        Entered Medline: 21 May 2004

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AB Large-scale transient transfection of mammalian **cells** is a recent and powerful technology for the fast production of milligram amounts of recombinant proteins (r-proteins). As many r-proteins used for therapeutic and structural studies are naturally **secreted** or engineered to be **secreted**, a cost-effective serum-free culture medium that allows their efficient expression and **purification** is required. In an attempt to design such a serum-free medium, the effect of nine protein hydrolysates on **cell** proliferation, transfection efficiency, and volumetric productivity was evaluated using green fluorescent protein (GFP) and human placental **secreted** alkaline phosphate (SEAP) as reporter genes. The suspension growing, serum-free adapted HEK293SF-3F6 **cell** line was stably transfected with an EBNA1-expression vector to increase protein expression when using EBV oriP bearing plasmids. Compared to our standard serum-free medium, concomitant addition of the **gelatin** peptone N3 and removal of BSA

**slightly** enhanced transfection efficiency and significantly increased volumetric productivity fourfold. Using the optimized medium formulation, transfection efficiencies between 40-60% were routinely obtained and SEAP production reached 18 mg/L(-1). To date, we have successfully produced and **purified** over fifteen r-proteins from 1-14-L bioreactors using this serum-free system. As examples, we describe the scale-up of two **secreted** his-tagged r-proteins Tie-2 and Neuropilin-1 **extracellular** domains (ED) in bioreactors. Each protein was successfully **purified** to >95% purity following a single **immobilized** metal affinity chromatography (IMAC) step. In contrast, **purification** of Tie-2 and Neuropilin-1 produced in serum-containing medium was much less efficient. Thus, the use of our new serum-free EBNA1 **cell** line with peptone-enriched serum-free medium significantly improves protein expression compared to peptone-less medium, and significantly increases their **purification** efficiency compared to serum-containing medium. This eliminates labor-intensive and expensive chromatographic steps, and allows for the simple, reliable, and extremely fast production of milligram amounts of r-proteins within 5 days posttransfection.

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L20 ANSWER 2 OF 19 MEDLINE on STN  
 ACCESSION NUMBER: 2001441245 MEDLINE  
 DOCUMENT NUMBER: PubMed ID: 11486861  
 TITLE: Ni(II)-based **immobilized** metal ion affinity chromatography of recombinant human prolactin from periplasmic Escherichia coli extracts.  
 AUTHOR: Ueda E K; Gout P W; Morganti L  
 CORPORATE SOURCE: Department of Biotechnology, Institute of Nuclear and Energy Research (IPEN-CNEN), Cidade Universitaria, Sao Paulo, Brazil.  
 SOURCE: Journal of chromatography. A, (2001 Jul 13) Vol. 922, No. 1-2, pp. 165-75.  
 Journal code: 9318488. ISSN: 0021-9673.  
 PUB. COUNTRY: Netherlands  
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
 LANGUAGE: English  
 FILE SEGMENT: Priority Journals  
 ENTRY MONTH: 200112  
 ENTRY DATE: Entered STN: 13 Aug 2001  
 Last Updated on STN: 21 Jan 2002  
 Entered Medline: 20 Dec 2001

AB A novel, two-step preparative technique is described for the **purification** of authentic recombinant human prolactin (rhPRL) **secreted** into the periplasm of transformed Escherichia coli **cells**. The first step is based on **immobilized** metal ion affinity chromatography of periplasmic extract, using Ni(II) as a relatively specific ligand for hPRL in this system. It gives superior resolution and yield than established ion-exchange chromatography. Size-exclusion chromatography is used for further **purification** to >99.5% purity. The **methodology** is reproducible, leading to 77% recovery. Identity and purity of the rhPRL were demonstrated using sodium dodecylsulphate-polyacrylamide electrophoresis, isoelectric focusing, mass spectrometry (matrix-assisted laser desorption ionization time-of-flight), radioimmunoassay, RP-HPLC and high-performance size-exclusion chromatography. In the Nb2 bioassay, the hormone showed a bioactivity of 40.9 IU/mg.

L20 ANSWER 3 OF 19 MEDLINE on STN  
 ACCESSION NUMBER: 92331575 MEDLINE

DOCUMENT NUMBER: PubMed ID: 1628601  
TITLE: Analysis of recombinant proteins by isoelectric focusing in **immobilized** pH gradients.  
AUTHOR: Bischoff R; Roecklin D; Roitsch C  
CORPORATE SOURCE: Transgene S.A., Protein Analytical Unit, Strasbourg, France.  
SOURCE: Electrophoresis, (1992 Apr) Vol. 13, No. 4, pp. 214-9. Journal code: 8204476. ISSN: 0173-0835.  
PUB. COUNTRY: GERMANY: Germany, Federal Republic of  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 199208  
ENTRY DATE: Entered STN: 4 Sep 1992  
Last Updated on STN: 4 Sep 1992  
Entered Medline: 20 Aug 1992

AB Isoelectric focusing in **immobilized** pH gradients (IEF-IPG) was used to analyze three different recombinant proteins. Recombinant leech hirudin (65 amino acids, three disulfide bonds) expressed in *Saccharomyces cerevisiae* as a **secreted** protein and **purified** by anion-exchange and reversed-phase chromatography proved to be homogeneous with regard to its isoelectric point (pI). In addition, the theoretical pI, calculated on the basis of the primary structure, corresponded precisely to the measured pI of 4.30. IEF-IPG was further employed to follow the stability of recombinant hirudin at pH 9, indicating that deamidation occurred under these conditions. A variant of recombinant human alpha 1-antitrypsin (AAT) (389 amino acids, one cysteine residue) expressed in *Escherichia coli* and **purified** by anion-exchange, metal chelate and hydrophobic-interaction chromatography appeared to be homogeneous by polyacrylamide **gel** electrophoresis under reducing and denaturing conditions as well as by various high performance liquid chromatography **methods**. However, some heterogeneity was detected by IEF-IPG between pH 5-6. The measured pI values of 5.43-5.58 were **slightly** lower than the calculated pI based on the primary structure (5.72). This indicated deamidations of Asn or Gln residues. A recombinant *Schistosoma mansoni* parasite antigen, p28 (210 amino acids, one cysteine residue) obtained after **intracellular** expression in *Saccharomyces cerevisiae* and affinity **purification** on glutathione agarose was analyzed by IEF-IPG in a pH 7.3-8.3 gradient. It appeared to be heterogeneous with regard to its pI, with the major component having a pI of 7.81 compared to the calculated value of 7.17. (ABSTRACT TRUNCATED AT 250 WORDS)

L20 ANSWER 4 OF 19 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN  
ACCESSION NUMBER: 2001:420002 BIOSIS  
DOCUMENT NUMBER: PREV200100420002  
TITLE: Functional characterization of recombinant chloroplast signal recognition particle.  
AUTHOR(S): Groves, Matthew R.; Mant, Alexandra; Kuhn, Audrey; Koch, Joachim; Duebel, Stefan; Robinson, Colin; Sinning, Irmgard [Reprint author]  
CORPORATE SOURCE: Structural Biology Programme, EMBL, Meyerhofstrasse 1, 69117, Heidelberg, Germany  
irmi.sinning@embl-heidelberg.de  
SOURCE: Journal of Biological Chemistry, (July 27, 2001) Vol. 276, No. 30, pp. 27778-27786. print. CODEN: JBCHA3. ISSN: 0021-9258.  
DOCUMENT TYPE: Article  
LANGUAGE: English  
ENTRY DATE: Entered STN: 5 Sep 2001

Last Updated on STN: 22 Feb 2002

AB The signal recognition particle (SRP) is a ubiquitous system for the targeting of membrane and **secreted** proteins. The chloroplast SRP (cpSRP) is unique among SRPs in that it possesses no RNA and is functional in post-translational as well as co-translational targeting. We have expressed and **purified** the two components of the Arabidopsis thaliana chloroplast signal recognition particle (cpSRP) involved in post-translational transport: cpSRP54 and the chloroplast-specific protein, cpSRP43. Recombinant cpSRP supports the efficient in vitro insertion of pea preLhcb1 into isolated thylakoid membranes. Recombinant cpSRP is a stable heterodimer with a molecular mass of approx 100 kDa as determined by analytical ultracentrifugation, **gel** filtration analysis, and dynamic **light** scattering. The interactions of the components of the recombinant heterodimer and pea preLhcb1 were probed using an **immobilized** peptide library (pepscan) approach. These data confirm two previously reported interactions with the L18 region and the third transmembrane helix of Lhcb1 and suggest that the interface of the cpSRP43 and cpSRP54 proteins is involved in substrate binding. Additionally, cpSRP components are shown to recognize peptides from the cleavable, N-terminal chloroplast transit peptide of preLhcb1. The interaction of cpSRP43 with cpSRP54 was probed in a similar experiment with a peptide library representing cpSRP54. The C terminus of cpSRP54 is essential for the formation of the stable cpSRP complex and cpSRP43 interacts with distinct regions of the M domain of cpSRP54.

L20 ANSWER 5 OF 19 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN  
ACCESSION NUMBER: 1994:271798 BIOSIS  
DOCUMENT NUMBER: PREV199497284798  
TITLE: Production of the immunoglobulin variable domain REI-v via a fusion protein synthesized and **secreted** by Staphylococcus carnosus.  
AUTHOR(S): Pschorr, Johannes; Bieseler, Barbara; Fritz, Hans-Joachim [Reprint author]  
CORPORATE SOURCE: Inst. Mol. Genet., Georg-August-Univ. Goettingen, Grisebachstr. 8, D-37077 Goettingen, Germany  
SOURCE: Biological Chemistry Hoppe-Seyler, (1994) Vol. 375, No. 4, pp. 271-280.  
CODEN: BCHSEI. ISSN: 0177-3593.  
DOCUMENT TYPE: Article  
LANGUAGE: English  
ENTRY DATE: Entered STN: 24 Jun 1994  
Last Updated on STN: 24 Jun 1994

AB REI-v - the variable domain of an immunoglobulin  $\kappa$  **light** chain - was produced by heterologous gene expression in a Gram-positive bacterium, **purified** to homogeneity and characterized. A host/vector combination based on **secretion** of Staphylococcus hyicus lipase by Staphylococcus carnosus was exploited. A gene encoding a fusion protein, composed of an aminoterminal portion of the pre-pro-peptide of S. hyicus lipase, a hexahistidine affinity tag, followed by the recognition sequence of IgA protease and REI-v was constructed. Expression of the fusion gene in S. carnosus causes selective **secretion** and accumulation of a soluble fusion protein in the culture medium (5-10 mg/l), which can be **purified** from the supernatant by **immobilized** metal ion affinity chromatography (IMAC). REI-v is released from the fusion protein with an additional threonine and proline residue at the aminoterminal (REI-vTP) by site-specific cleavage with IgA protease and can be separated from the hexahistidine-tagged fusion partner and the protease by a second passage through an IMAC **gel** matrix. Like authentic REI-v, the isolated

protein (gt 1 mg/l culture medium) migrates as a dimer in gel filtration chromatography and undergoes cooperative, reversible unfolding in urea. The isolated immunoglobulin REI-vTP and authentic REI-v have indistinguishable free energies of unfolding (approx. 26 kJ/mol, 6.3 kcal/mol).

L20 ANSWER 6 OF 19 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 2003180981 EMBASE  
 TITLE: Construction, expression and tumor targeting of a single-chain Fv against human colorectal carcinoma.  
 AUTHOR: Fang J.; Jin H.-B.; Song J.-D.  
 CORPORATE SOURCE: Prof. J.-D. Song, Key Lab of Cell Biology, Ministry of Public Health of China, China Medical University, 92 Beier Road, Shenyang 110001, Liaoning Province, China. jdsong@mail.cmu.edu.cn  
 SOURCE: World Journal of Gastroenterology, (15 Apr 2003) Vol. 9, No. 4, pp. 726-730. .  
 Refs: 40  
 ISSN: 1007-9327 CODEN: WJGAF2  
 COUNTRY: China  
 DOCUMENT TYPE: Journal; Article  
 FILE SEGMENT: 048 Gastroenterology  
 016 Cancer  
 030 Pharmacology  
 022 Human Genetics  
 037 Drug Literature Index  
 LANGUAGE: English  
 SUMMARY LANGUAGE: English  
 ENTRY DATE: Entered STN: 22 May 2003  
 Last Updated on STN: 22 May 2003

AB Aim: A single-chain antibody fragment, ND-lscFv, against human colorectal carcinoma was constructed and expressed in E.coli, and its biodistribution and pharmacokinetic properties were studied in mice bearing tumor.  
**Methods:** VH and VL genes were amplified from hybridoma cell IC-2, **secreting** monoclonal antibody ND-1, by RT-PCR, and connected by linker (Gly(4)Ser)(3) to form scFv gene, which was cloned into expression vector pET 28a(+) and finally expressed in E.coli. The expressed product ND-lscFv was **purified** by metal affinity chromatography using Ni-NTA, its purity and biological activity were determined using SDS-PAGE and ELISA. ND-lscFv was labeled with (99m)Tc, and then injected into mice bearing colorectal carcinoma xenograft for pharmacokinetic study in vivo. Results: SDS-PAGE analysis showed that the relative molecular weight of recombinant protein was 30kDa with purity of 94 %. ELIAS assay revealed that ND-lscFv retained the immunoactivity of parent mAb, being capable of binding specifically to human colorectal carcinoma **cell** line expressing associated antigen. Radiolabeled ND-lscFv exhibited rapid tumor targeting, with specific distribution in mice bearing colorectal carcinoma xenograft observed as early as 1 h following injection. In vivo pharmacokinetic studies also demonstrated that ND-lscFv had very rapid plasma clearance ( $T(1/2)\alpha$  of 5.7 min,  $T(1/2)\beta$  of 2.6 h). Conclusion: ND-lscFv shows significant immunoactivity, and better pharmacokinetic and biodistribution characteristics compared with intact mAbs, demonstrating the possibility as a carrier for tumor-**imaging**.

L20 ANSWER 7 OF 19 WPIDS COPYRIGHT 2006 THE THOMSON CORP on STN  
 ACCESSION NUMBER: 2005-618107 [63] WPIDS  
 DOC. NO. CPI: C2005-185716 [63]  
 TITLE: **Purifying one or more selected cells**

by contacting **cells immobilized** in proximity to a capture matrix with an agent that selectively binds to the product, illuminating a population of the **cells** and **irradiating** the non-selected **cells**

DERWENT CLASS:

B04; D16

INVENTOR:

EISFELD T M; FIECK A; HANANIA E G; KOLLER M R

PATENT ASSIGNEE:

(EISF-I) EISFELD T M; (FIEC-I) FIECK A; (HANA-I) HANANIA E G; (KOLL-I) KOLLER M R; (ONCO-N) ONCOSIS LLC

COUNTRY COUNT:

107

PATENT INFO ABBR.:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN IPC
US 20050202558	A1	20050915	(200563)*	EN	18[4]	
WO 2005090555	A1	20050929	(200564)	EN		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
US 20050202558	A1	US 2004-801931	20040315
WO 2005090555	A1	WO 2005-US8347	20050314

PRIORITY APPLN. INFO: US 2004-801931 20040315

AN 2005-618107 [63] WPIDS

AB US 20050202558 A1 UPAB: 20051223

NOVELTY - **Purifying** one or more selected **cells** comprises:

- (1) contacting **cells immobilized** in proximity to a capture matrix with an agent that selectively binds to the product;
- (2) illuminating a population of the **cells**;
- (3) detecting two or more properties of **light** directed from the frame; and
- (4) **irradiating** the non-selected **cells**.

DETAILED DESCRIPTION - **Purifying** one or more selected **cells** comprises:

- (1) contacting **cells immobilized** in proximity to a capture matrix, the capture matrix capable of localizing a product **secreted** by one or more of the **cells**, with an agent that selectively binds to the product, the agent capable of generating a signal detectable as a property of **light**;
- (2) illuminating a population of the **cells**, the population contained in a frame;
- (3) detecting two or more properties of **light** directed from the frame, where a first property of **light** identifies substantially all **cells** of the population, and the second property of **light** identifies product localized to the capture matrix;
- (4) locating (1) substantially all **cells** of the population with reference to the detected first property of **light**, and (2) one or more selected **cells** with reference to the detected second property of **light**; and
- (5) **irradiating** the non-selected **cells**, where each non-selected **cell** receives a substantially lethal dose of **radiation**, whereby one or more selected **cells** having a desired product **secretion** profile are **purified**.

USE - The **method** is useful in **purifying** one or more selected **cells** (claimed).

L20 ANSWER 8 OF 19 WPIDS COPYRIGHT 2006 THE THOMSON CORP on STN  
 ACCESSION NUMBER: 2005-346863 [35] WPIDS  
 DOC. NO. CPI: C2005-107404 [35]  
 TITLE: New reverse transcription incompetent lipoparticle  
 comprising a viral protein component consisting of a  
 viral structural protein and an unmodified  
**cellular** protein, useful in preparing a vaccine  
 against cancer or infections  
 DERWENT CLASS: B04; D16  
 INVENTOR: DORANZ B J; GREENE T A; ROSS E; ROSS E D; WILLIS S;  
 DORANZ B; GREENE T  
 PATENT ASSIGNEE: (DORA-I) DORANZ B J; (GREE-I) GREENE T A; (INTE-N)  
 INTEGRAL MOLECULAR INC; (ROSS-I) ROSS E; (WILL-I) WILLIS  
 S  
 COUNTRY COUNT: 107

## PATENT INFO ABBR.:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN IPC
WO 2005042695	A2	20050512	(200535)*	EN	305	[30]
US 20050123563	A1	20050609	(200538)	EN		
EP 1660638	A2	20060531	(200636)	EN		
AU 2004286197	A1	20050512	(200663)	EN		

## APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2005042695	A2	WO 2004-US24984	20040730
US 20050123563	A1 Provisional	US 2003-491477P	20030730
US 20050123563	A1 Provisional	US 2003-491633P	20030730
US 20050123563	A1 Provisional	US 2003-498755P	20030829
US 20050123563	A1 Provisional	US 2003-502478P	20030912
US 20050123563	A1 Provisional	US 2003-509575P	20031007
US 20050123563	A1 Provisional	US 2003-509608P	20031007
US 20050123563	A1 Provisional	US 2003-509677P	20031007
US 20050123563	A1	US 2004-901399	20040728
EP 1660638	A2	EP 2004-816792	20040730
EP 1660638	A2	WO 2004-US24984	20040730
AU 2004286197	A1	AU 2004-286197	20040730

## FILING DETAILS:

PATENT NO	KIND	PATENT NO
EP 1660638	A2 Based on	WO 2005042695 A
AU 2004286197	A1 Based on	WO 2005042695 A

PRIORITY APPLN. INFO: US 2003-509677P 20031007  
 US 2003-491633P 20030730  
 US 2003-491477P 20030730  
 US 2003-498755P 20030829  
 US 2003-502478P 20030912  
 US 2003-509608P 20031007  
 US 2003-509575P 20031007  
 US 2004-901399 20040728

AN 2005-346863 [35] WPIDS  
 AB WO 2005042695 A2 UPAB: 20051222



NOVELTY - A new lipoparticle, which is reverse transcription incompetent, comprises a viral protein component consisting essentially of a viral structural protein and a **cellular** protein which is an unmodified protein.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

- (1) a composition comprising an isolated lipoparticle or an array of lipoparticles attached to a surface attached to a biosensor surface;
- (2) a **method** of identifying modulators of a GPCR;
- (3) a **method** for producing a lipoparticle;
- (4) a chimeric viral vector comprising adenoviral nucleic acid and retroviral nucleic acid, provided that the retroviral nucleic acid comprises a sequence encoding Gag, but does not comprise a sequence encoding the envelope, promoter, or packaging signal of the retrovirus;
- (5) a **method** of eliciting an immune response in a subject;
- (6) a **method** of assessing the binding interaction of a protein with a ligand;
- (7) a **method** of identifying potential ligands of a protein;
- (8) a **method** of identifying a compound that affects binding between a ligand and a protein;
- (9) a **method** of detecting a ligand of a protein in a test sample;
- (10) an immunogen comprising the lipoparticle;
- (11) a **method** of eliciting an immune response to a protein;
- (12) a **method** of determining the structure of a membrane protein or protein;
- (13) a **method** of detecting an infectious pathogen in a sample;
- (14) a **method** of determining the presence of a substance in a sample;
- (15) a **method** of identifying an inhibitor of a binding activity of a substance to a membrane protein;
- (16) a **method** for spotting lipoparticles, viruses, or virus-like particles in an array format onto a surface;
- (17) a **method** of identifying a binding partner of a membrane protein;
- (18) a **method** for determining membrane protein function in a lipoparticle, virus, or virus-like particle comprising a membrane protein and a detectable agent;
- (19) a **method** of identifying a stimulator of a membrane protein;
- (20) a **method** of identifying an inhibitor of a known stimulator of an ion channel protein or a transporter protein within a lipoparticle, where the lipoparticle comprises an ion channel or transporter;
- (21) a **method** of detecting changes in ion concentration in a location;
- (22) an immunogenic composition comprising the lipoparticle comprising a protein of interest and at least one immunostimulatory component;
- (23) a **method** of producing antibodies against a protein;
- (24) a **method** of identifying a binding partner of a membrane protein;
- (25) a **method** of transfecting a protein into a **cell**;
- (26) a **method** of correcting a protein defect in an individual;

(27) a particle comprising a fluorophore that changes fluorescence in response to pH, membrane potential, oxidation state, NO level, ion concentration, ATP concentration and/or protein interaction in size, where the particle is less than 1mu;

(28) a **method** of incorporating a molecule into a lipoparticle, virus or a virus-like particle;

(29) a **method** of inducing pores in a lipoparticle;

(30) a **method** of attaching a molecule to a lipoparticle, virus, or virus-like particle;

(31) a **method** of determining binding of a compound to a lipoparticle, virus, or virus-like particle;

(32) a **method** of detecting the presence of an antigen in a sample;

(33) a **method** of hybridizing an oligonucleotide to a target sequence in a lipoparticle, virus, or virus-like particle;

(34) a **method** of detecting lipoparticle fusion;

(35) a **method** for calculating the number of lipoparticles, viruses, or virus-like particles in a sample;

(36) a **method** for calculating the quantity of particles, comprising lipoparticles, viruses, or virus-like particles;

(37) a **method** for detecting the structural integrity of a membrane protein within a particle;

(38) a **method** for determining the purity of a particle, where the particle is a lipoparticle, virus, or virus-like particle preparation;

(39) a **method** of detecting the presence of an antigen in a sample; and

(40) a device comprising at least one lipoparticle and used for detecting the presence of an antigen in a sample.

ACTIVITY - Cytostatic; Virucide; Antibacterial. No biological data given.

MECHANISM OF ACTION - Vaccine.

USE - The lipoparticle is useful in preparing a composition for eliciting an immune response (claimed) against cancer or viral or bacterial infections.

L20 ANSWER 9 OF 19 WPIDS COPYRIGHT 2006 THE THOMSON CORP on STN  
 ACCESSION NUMBER: 2004-758031 [74] WPIDS  
 DOC. NO. CPI: C2004-266076 [74]  
 DOC. NO. NON-CPI: N2004-598607 [74]  
 TITLE: Screening for **secretion** of polypeptide of interest by culturing **cell** expressing glycosylated polypeptide, contacting sample from culture with **immobilized** lectin, isolating **immobilized** lectin retaining polypeptide, releasing polypeptide  
 DERWENT CLASS: A96; B04; D16; S03  
 INVENTOR: SCHNORR K M  
 PATENT ASSIGNEE: (NOVO-C) NOVOZYMES AS  
 COUNTRY COUNT: 106

#### PATENT INFO ABBR.:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN IPC
WO 2004090549	A1	20041021	(200474)*	EN	39	[0]

#### APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
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WO 2004090549 A1

WO 2004-DK246 20040405

PRIORITY APPLN. INFO: DK 2003-577 20030411

AN 2004-758031 [74] WPIDS

AB WO 2004090549 A1 UPAB: 20050707

NOVELTY - Screening for **secretion** of a polypeptide of interest, involves providing a host **cell** expressing and **secreting** a glycosylated polypeptide of interest and culturing host **cell**, contacting in solution and in a compartment a liquid sample from culture comprising polypeptide with **immobilized** lectin compound capable of binding to the polypeptide, isolating **immobilized** lectin retaining polypeptide and releasing polypeptide from **immobilized** lectin.

DETAILED DESCRIPTION - Screening for **secretion** of a polypeptide of interest, involves providing a host **cell** expressing and **secreting** a glycosylated polypeptide of interest and culturing host **cell**, contacting in solution and in a compartment a liquid sample from culture comprising polypeptide with **immobilized** lectin compound capable of binding to the polypeptide, isolating **immobilized** lectin retaining polypeptide and releasing polypeptide from **immobilized** lectin.

Screening (M1) for **secretion** of a polypeptide of interest, involves:

(a) providing a host **cell** expressing and **secreting** a glycosylated polypeptide of interest and culturing the host **cell** under conditions promoting the expression; and

(b) contacting in solution and in a compartment a liquid sample from (a) comprising the glycosylated polypeptide of interest with an **immobilized** lectin compound capable of binding to the glycosylated polypeptide of interest, under conditions where binding capacity of the **immobilized** lectin compound per compartment volume is at least 10 ng polypeptide/300 microl compartment volume, isolating the **immobilized** lectin compound retaining the polypeptide of interest and releasing the polypeptide of interest from the **immobilized** lectin compound.

USE - (M1) is useful for screening for **secretion** of a polypeptide of interest (claimed).

ADVANTAGE - (M1) enables rapid and convenient screening of samples from a recombinant library of **secreted** polypeptide of interest or cDNA library, expressed in a host **cell**, in a high throughput format.

L20 ANSWER 10 OF 19 WPIDS COPYRIGHT 2006 THE THOMSON CORP on STN

ACCESSION NUMBER: 2003-721774 [68] WPIDS

DOC. NO. CPI: C2003-198648 [68]

TITLE: Preparing modified manganese dismutase, useful for treating disorders, e.g. cancer, associated with superoxide radicals, by growing LSA **cells** in protein-free medium

DERWENT CLASS: B04; D16; D21; D22

INVENTOR: MANCINI A

PATENT ASSIGNEE: (NAST-N) IST NAZ STUDIO E CURA DEI TUMORI

COUNTRY COUNT: 101

PATENT INFO ABBR.:

PATENT NO	KIND DATE	WEEK	LA	PG	MAIN IPC
WO 2003072768	A2 20030904	(200368)*	EN	24	[4]

AU 2003208771	A1 20030909 (200428)	EN
EP 1481056	A2 20041201 (200478)	EN
AU 2003208771	A8 20051020 (200615)	EN

## APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2003072768	A2	WO 2003-EP2017	20030227
AU 2003208771	A1	AU 2003-208771	20030227
EP 1481056	A2	EP 2003-706586	20030227
EP 1481056	A2	WO 2003-EP2017	20030227
AU 2003208771	A8	AU 2003-208771	20030227

## FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 2003208771	A1	WO 2003072768 A
EP 1481056	A2	WO 2003072768 A
AU 2003208771	A8	WO 2003072768 A

## PRIORITY APPLN. INFO: IT 2002-MI404 20020228

AN 2003-721774 [68] WPIDS

AB WO 2003072768 A2 UPAB: 20050601

NOVELTY - Preparing (M1) modified manganese dismutase (A) by growing lipid-bound sialic acid (LSA) (Deutsche Sammlung von Mikroorganismen und Zellkulturen GmbH (DSMZ) 2029) **cells** in protein-free medium for at least 24 hours, then **purification** of (A) from conditioned medium by chromatography, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for:

(1) (A) that has molecular weight 28-33 kD measured by sodium dodecylsulfate polyacrylamide **gel** electrophoresis; and

(2) (A) produced by M1.

ACTIVITY - Cytostatic; Antiulcer; Dermatological; Vulnerary; Antibacterial; Immunosuppressive; Neuroprotective; Cardiant; Antidiabetic; Analgesic; Virucide; Antiinflammatory.

Mammary cancers were induced in mice using Bittner virus, then the animals injected (daily for 10 days) with 5 ng of (A) and after 15 days the tumors were examined. All tumors were completely necrotic with no metastases to the lungs.

MECHANISM OF ACTION - (A) catalyzes decomposition of superoxide radicals.

USE - (A) is useful for:

(i) treatment and prevention of tumors and damage caused by ionizing **radiation**; and

(ii) treating skin lesions, particularly decubitus or torpid ulcers and burns; septic and traumatic shock; central nervous system degeneration, cardiovascular disease, diabetic neuropathy, post-herpetic neuritis and malignant hyperthermia.

It can also be used in cosmetics (to reduce skin wrinkles, increase tissue tone and prevent skin inflammation), and for preservation of organs intended for transplantation.

ADVANTAGE - Unlike unmodified Mn dismutase, (I) is produced in soluble form and **secreted**, and when formulated with cis-platin provides a synergistic increase in antitumor effect.

L20 ANSWER 11 OF 19 WPIDS COPYRIGHT 2006

THE THOMSON CORP on STN

ACCESSION NUMBER: 2003-645873 [61] WPIDS

DOC. NO. CPI: C2003-176589 [61]

TITLE: **Purifying** and/or isolating granulocyte colony stimulating factor (G-CSF), useful for treating neutropenia, thrombotic illness, by subjecting the mixture containing the G-CSF to **immobilized** metal affinity chromatography

DERWENT CLASS: A96; A97; B04; D16

INVENTOR: GABERC P; GABERC P V; GABERC POREKAR V; MENART V; POREKAR V G

PATENT ASSIGNEE: (GABE-I) GABERC P V; (LEKT-C) LEK PHARM DD; (MENA-I) MENART V

COUNTRY COUNT: 101

PATENT INFO ABBR.:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN IPC
WO 2003051922	A1	20030626	(200361)*	EN	35[5]	
AU 2002366275	A1	20030630	(200420)	EN		
EP 1458757	A1	20040922	(200462)	EN		
KR 2004071212	A	20040811	(200481)	KO		
BR 2002015191	A	20041116	(200501)	PT		
NO 2004002967	A	20040907	(200517)	NO		
HU 2004002547	A2	20050329	(200528)	HU		
US 20050159589	A1	20050721	(200548)	EN		
CN 1606568	A	20050413	(200554)	ZH		
IN 2004001605	P1	20050401	(200559)	EN		
JP 2005525304	W	20050825	(200560)	JA	21	
MX 2004006076	A1	20050301	(200568)	ES		
ZA 2004004291	A	20050928	(200570)	EN	42	
NZ 533305	A	20051125	(200625)	EN		

## APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2003051922	A1	WO 2002-EP13810	20021205
AU 2002366275	A1	AU 2002-366275	20021205
BR 2002015191	A	BR 2002-15191	20021205
CN 1606568	A	CN 2002-825465	20021205
EP 1458757	A1	EP 2002-804876	20021205
EP 1458757	A1	WO 2002-EP13810	20021205
BR 2002015191	A	WO 2002-EP1381	20021205
NO 2004002967	A	WO 2002-EP13810	20021205
HU 2004002547	A2	WO 2002-EP13810	20021205
US 20050159589	A1	WO 2002-EP13810	20021205
IN 2004001605	P1	WO 2002-EP13810	20021205
JP 2005525304	W	WO 2002-EP13810	20021205
MX 2004006076	A1	WO 2002-EP13810	20021205
JP 2005525304	W	JP 2003-552802	20021205
HU 2004002547	A2	HU 2004-2547	20021205
ZA 2004004291	A	ZA 2004-4291	20040601
IN 2004001605	P1	IN 2004-DN1605	20040608
KR 2004071212	A	KR 2004-709409	20040617
US 20050159589	A1	US 2004-499315	20040617
MX 2004006076	A1	MX 2004-6076	20040618
NO 2004002967	A	NO 2004-2967	20040714
NZ 533305	A	NZ 2002-533305	20021205
NZ 533305	A	WO 2002-EP13810	20021205

## FILING DETAILS:

PATENT NO	KIND		PATENT NO	
AU 2002366275	A1	Based on	WO 2003051922	A
EP 1458757	A1	Based on	WO 2003051922	A
BR 2002015191	A	Based on	WO 2003051922	A
HU 2004002547	A2	Based on	WO 2003051922	A
JP 2005525304	W	Based on	WO 2003051922	A
MX 2004006076	A1	Based on	WO 2003051922	A
NZ 533305	A	Based on	WO 2003051922	A

PRIORITY APPLN. INFO: SI 2001-322 20011219

AN 2003-645873 [61] WPIDS

AB WO 2003051922 A1 UPAB: 20060120

NOVELTY - **Purifying** and/or isolating biologically active granulocyte colony stimulating factor (G-CSF) comprising providing a mixture comprising a biologically active form of G-CSF in the presence of an impurity, and subjecting the mixture to **immobilized** metal affinity chromatography (IMAC), is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for:

(1) a biologically active G-CSF with a purity of greater than 99%;  
and

(2) a pharmaceutical composition comprising a therapeutic amount of the biologically active G-CSF, and auxiliary substances.

ACTIVITY - Immunomodulator; Cytostatic; Vulnerary; Cerebroprotective; Thrombolytic; Antibacterial; Antiinflammatory.

No biological data given.

MECHANISM OF ACTION - Gene therapy.

USE - The **method** and biologically active G-CSF are useful for producing a medicament for indications selected from neutropenia, neutropenia-related clinical sequelae, reduction of hospitalization for febrile neutropenia after chemotherapy, mobilization of hematopoietic progenitor **cells** as an alternative to donor leukocyte infusion, chronic neutropenia, neutropenic and non-neutropenic infections, transplant recipients, chronic inflammatory conditions, sepsis and septic shock, reduction of risk/morbidity/mortality/number of days of hospitalization in neutropenic and non-neutropenic infections, prevention of infection and infection-related complications in neutropenic and non-neutropenic patients, prevention of nosocomial infections, enteral administration in neonates, enhancing the immune system in neonates, improving the clinical outcome in intensive care unit patients and critically ill patients, wound/skin ulcers/burns healing and treatment, intensification of chemotherapy and/or radiotherapy, pancytopenia, increase of anti-inflammatory cytokines, shortening of intervals of high-dose chemotherapy by the prophylactic employment of filgrastim, potentiation of the anti-tumor effects of photodynamic therapy, prevention and treatment of illness caused by different cerebral dysfunctions, treatment of thrombotic illness and their complications, and post-**irradiation** recovery of erythropoiesis (claimed).

ADVANTAGE - The invention provides improved **purification** and/or isolation of G-CSF, and biologically active G-CSF in highly **purified** and active form.

L20 ANSWER 12 OF 19 WPIDS COPYRIGHT 2006 THE THOMSON CORP on STN

ACCESSION NUMBER: 2002-426103 [45] WPIDS

DOC. NO. CPI: C2002-120735 [45]

DOC. NO. NON-CPI: N2002-335056 [45]

TITLE: Novel **purified** nectin-3 and nectin-4 polypeptides which bind to nectin-1, useful for treating or preventing heart failure, malaria, glomerulonephritis,

endometriosis, leukemia, asthma, allergy, edema, sepsis, stroke  
 DERWENT CLASS: B04; D16; S03  
 INVENTOR: BAUM P; BAUM P R; FANSLOW III W; FANSLOW W C; LOFTON T;  
 LOFTON T E; SORENSSEN E; SORENSSEN E A; YOUAKIM A  
 PATENT ASSIGNEE: (BAUM-I) BAUM P R; (FANS-I) FANSLOW W C; (IMMV-C) IMMUNEX  
 CORP; (LOFT-I) LOFTON T E; (SORE-I) SORENSSEN E A;  
 (YOUA-I) YOUAKIM A  
 COUNTRY COUNT: 96

## PATENT INFO ABBR.:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN IPC
WO 2002028902	A2	20020411	(200245)*	EN	141	[0]
AU 2002013053	A	20020415	(200254)	EN		
US 20030044893	A1	20030306	(200320)	EN		
EP 1325032	A2	20030709	(200345)	EN		
JP 2004528008	W	20040916	(200461)	JA	229	
MX 2003002479	A1	20040601	(200504)	ES		

## APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2002028902	A2	WO 2001-US31392	20011005
US 20030044893	A1 Provisional	US 2000-238557P	20001005
EP 1325032	A2	EP 2001-981410	20011005
US 20030044893	A1	US 2001-972268	20011005
EP 1325032	A2	WO 2001-US31392	20011005
JP 2004528008	W	WO 2001-US31392	20011005
MX 2003002479	A1	WO 2001-US31392	20011005
AU 2002013053	A	AU 2002-13053	20011005
JP 2004528008	W	JP 2002-532484	20011005
MX 2003002479	A1	MX 2003-2479	20030320

## FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 2002013053	A	WO 2002028902 A
EP 1325032	A2	WO 2002028902 A
JP 2004528008	W	WO 2002028902 A
MX 2003002479	A1	WO 2002028902 A

PRIORITY APPLN. INFO: US 2000-238557P 20001005  
 US 2001-972268 20011005

AN 2002-426103 [45] WPIDS

AB WO 2002028902 A2 UPAB: 20050526

NOVELTY - A substantially **purified** nectin (3alpha, 3beta and 3gamma and nectin-4) polypeptide (I) which has a sequence that is 80% identical to a fully defined sequence (PS) of 542, 549, 504, 510, 437, 511, 497, 402, or 498 amino acids as given in specification, where the polypeptide binds to nectin 1; or a fragment of the above mentioned polypeptide, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are included for the following:

(1) a substantially **purified** soluble polypeptide (II) which is a polypeptide comprising a sequence that is at least 80% identical to **extracellular** domain of PS, where the polypeptide

binds to nectin-1, or is a fragment of the above mentioned polypeptide that binds to nectin 1, and that inhibits endothelial **cell** migration;

- (2) a composition (III) comprising (I) or (II) and a carrier;
- (3) an isolated polynucleotide (IV) encoding (I) or (II);
- (4) an isolated polynucleotide (V) which comprises:
  - (a) a fully defined sequence (NS) of 3147 (S1), 1650 (S3), 1650 (S5), 2603 (S7), 1533 (S9), 1533 (S11), 1314 (S30), 1533 (S32), 1660 (S33) or 1838 (S35) nucleotides as given in specification;
  - (b) comprises a sequence of nucleotides x1-1212 of (S3) or (S5), where x1 is a nucleotide between 1 and 115 and nucleotide 172-456, 172-750, 172-1026, 172-1212, 222-456, 222-750, 222-1026, 222-1212, 567-750, 567-1026, 567-1212, 861-1026 or nucleotides 861-1212 of (S3) or (S5);
  - (c) comprises a sequence of nucleotides x1-1098 of (S9) or (S11), where x1 is a nucleotide between 1 and 115 and nucleotide 172-456, 172-750, 172-1026, 172-1098, 222-456, 222-750, 222-1026, 222-1098, 567-750, 567-1026, 567-1098, 861-1026 or nucleotides 861-1098 of (S9) or (S11);
  - (d) comprises a sequence of nucleotides 79-1047 of (S32) or (S33);
  - (e) is a polynucleotide that hybridizes under moderate to highly stringent conditions to (a), (b), (c), or (d), and encoding a polypeptide that binds to nectin-1;
  - (f) is a polynucleotide having a sequence complementary to NS; or
  - (g) is any of nucleotide sequence (a)-(f), where T can also be U;
- (5) an isolated polynucleotide comprising (V) operably linked to a polynucleotide encoding Fc polypeptide, a leucine zipper polypeptide or a peptide linker;
- (6) an expression vector (VI) comprising (IV) or (V);
- (7) a recombinant host **cell** (VII) genetically engineered to contain (IV);
- (8) preparation of (I) or (II);
- (9) a polypeptide produced by culturing (VII) under conditions to promote the expression of the polypeptide;
- (10) a substantially **purified** antibody (VIII) that binds to (I) or (II); and
- (11) modulating (M1) **cellular** proliferation or migration by contacting **cell** with an agent that modulates nectin-1 activity or expression.

ACTIVITY - Antiinflammatory; Antibacterial; Antidiabetic; Ophthalmological; Antiasthmatic; Antiallergic; Cytostatic; Immunosuppressive; Virucide; Vasotropic; Antiatherosclerotic; Cerebroprotective; Thrombolytic; Protozoacide; Tuberculostatic; Cardiant; Antiulcer; Nephrotropic; Vulnerary; Tranquilizer; Hepatotrophic; Antigout; Antirheumatic; Antiarthritic; Gynecological; Antiinfertility.

MECHANISM OF ACTION - Angiogenesis inhibitor; **cell** adhesion activity, adherens junction formation activity, epithelial or endothelial barrier function activity, endothelial proliferation or migration activity, or viral polypeptide binding activity modulator; nectin-1 activity modulator. A mouse corneal pocket assay was used to quantitate the inhibition of angiogenesis by nectin-3-Fc polypeptides in vivo. In this assay, agents to be tested for angiogenic or anti-angiogenic activity were **immobilized** in a slow release form in a hydron pellet, which was implanted into micropockets created in the corneal epithelium of anesthetized mice. Vascularization was measured. Hydron pellets, the pellets were surgically implanted into corneal stromal micropockets created in 6-8 week old male C57BL mice. After five days, at the peak of neovascular response to basic fibroblast growth factor (bFGF), the corneas were photographed at an incipient angle of 35-50degrees from the polar axis in the meridian containing the pellet. **Images**



were digitized and processed to delineate established microvessels by hemoglobin content. **Image** analysis software was used to calculate the fraction of the corneal **image** that was vascularized, the vessel density within the vascularized area, and the vessel density within the total cornea. The inhibition of bFGF-induced corneal angiogenesis, as a function of the dose of sol(soluble)Nectin3-Fc polypeptide, was determined. The data demonstrated that solNectin3-Fc (alpha or beta) having a fully defined sequence of 634 or 595 amino acids as given in specification, respectively, blocked FGF-induced angiogenesis in the mouse corneal assay.

USE - (I) or (II) is useful for: designing an inhibitor or binding agent to (I) or (II) which involves determining three-dimension structure of the polypeptide, analyzing three-dimensional structure for binding sites of substrates or ligands, designing a molecule that is predicted to interact with the polypeptide, and determining inhibitory or binding activity of the molecule; identifying an agent that modulates the activity of (I) or (II) which involves contacting an agent with (I) or (II) under conditions such that the agent and the polypeptide interact and determining the activity of the polypeptide in the presence of an agent compared to a control, where a change in activity is indicative of an agent that modulates the polypeptide activity. The agent is preferably an antibody, a small molecule, a peptide, or a peptidomimetic the activity of (I) or (IV) such as nectin-1 binding activity, **cell** adhesion activity, adherens junction formation activity, epithelial or endothelial barrier function activity, endothelial-, epithelial-, or smooth muscle **cell**-proliferation or migration activity or viral polypeptide binding activity; modulating an activity of nectin-1 polypeptide; identifying agent that modulates binding between nectin-1 polypeptide and (I) or (IV) which involves contacting a sample containing nectin-1 polypeptide with the agent and measuring the interaction of the nectin-1 polypeptide with the polypeptide compared to a control sample, where a change in the binding between the nectin-1 polypeptide and the polypeptide compared to the control is indicative of an agent that modulates binding. The agent is a polypeptide, peptide, an antibody, peptidomimetic or a small molecule; increasing adherens junction formation activity, epithelial or endothelial barrier function activity, or **cell** adhesion activity which involves contacting a **cell** with (I) or (II); or decreasing **cell** adhesion activity, adherens junction formation activity, epithelial or endothelial barrier function activity, endothelial-, epithelial-, or smooth muscle **cell** proliferation or migration activity, or viral polypeptide activity which involves contacting a **cell** with (I) or (II). (I), (II) or (VIII) is useful for treating a disease associated with **cell** adhesion activity, adherens junction formation activity, epithelial or endothelial barrier function activity, endothelial proliferation or migration activity, viral polypeptide binding activity, or angiogenesis in subject. The epithelial or endothelial barrier function disorder which is treated by the above mentioned **method** is inflammation, sepsis, edema, diabetic retinopathy, asthma, allergy, allograft rejection, metastasis of cancer **cells**, **paracellular** transport disorders such as magnesium transport defects in the kidney or inflammatory bowel disease. The polypeptide employed in all the above mentioned **methods** has a fully defined sequence of 634, 595, 426, 387 or 580 amino acids as given in specification. The polypeptide is preferably in the form of multimer, e.g. a dimer or trimer, and comprises Fc polypeptide, a leucine zipper or a peptide linker. (II) (which further comprises Fc, leucine zipper or peptide linker polypeptide) is useful for modulating **cellular** proliferation or migration. (II) is also useful for inhibiting angiogenesis in a mammal, and treating endothelial proliferation, migration or angiogenic condition of a tissue or a subject, such as

ischemia, atherosclerosis, ischemia-reperfusion injury, stroke, thrombosis, restenosis, or tumor growth. The polypeptide is contacted with a tissue or a subject in vitro or in vivo. (II) is also useful for treating herpesvirus infection. (M1) is useful for modulating proliferation or migration of an endothelial **cell**, an epithelial **cell** or a smooth muscle **cell** (preferably, vascular smooth muscle **cell**) (all claimed). (I) or (II) is useful for **purifying** polypeptides and measuring their activity as delivery agents, therapeutic and research reagents, molecular weight and isoelectric focusing markers, etc. (IV) or (V) is useful as probes or primers, in diagnostic techniques, as markers for tissues in which the corresponding polypeptide is expressed, as chromosome markers or tags, as molecular weight markers or Southern **gels**, as an antigen to raise anti-DNA antibodies or elicit another immune response and for gene therapy, etc. (I), (II) or (VII) are useful for treating bacterial, viral or protozoan infections and their complications, e.g., malaria, bacterial or viral meningitis, tuberculosis, influenza, cardiovascular disorders such as myocarditis, heart failure, endocrine disorders, e.g., juvenile onset diabetes; gastrointestinal system disorders e.g., pancreatitis, ulcerative colitis; disorders of genitourinary system e.g., glomerulonephritis; hematologic and oncologic disorders e.g., leukemia, glioma, solid tumors; injuries to head or spinal cord; liver disorder such as hepatitis; pulmonary disorder such as emphysema, allergic rhinitis; rheumatic disorder such as gout, rheumatoid arthritis; female reproductive system disorders such as endometriosis, multiple implant failure/infertility, and for preparing therapeutic compositions for the treatment of these disorders.

L20 ANSWER 13 OF 19 WPIDS COPYRIGHT 2006 THE THOMSON CORP on STN  
 ACCESSION NUMBER: 2002-393728 [42] WPIDS  
 DOC. NO. CPI: C2002-110695 [42]  
 TITLE: Novel recombinant monoclonal antibody with 4G10-hybridoma type specificity useful in diagnostic procedures, especially for detection of phosphotyrosine-containing proteins in a sample  
 DERWENT CLASS: B04; D16  
 INVENTOR: EISINGER D; ESINGER D; JELINEK T; LAMARCHE A; STILES L  
 PATENT ASSIGNEE: (UPST-N) UPSTATE BIOTECHNOLOGY INC  
 COUNTRY COUNT: 96

## PATENT INFO ABBR.:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN IPC
WO 2002018443	A2	20020307	(200242)*	EN	60	[5]
AU 2001086896	A	20020313	(200249)	EN		
EP 1313863	A2	20030528	(200336)	EN		
JP 2004526408	W	20040902	(200457)	JA	92	
US 6824989	B1	20041130	(200479)	EN		

## APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2002018443	A2	WO 2001-US26926	20010830
US 6824989	B1	US 2000-653755	20000901
AU 2001086896	A	AU 2001-86896	20010830
EP 1313863	A2	EP 2001-966376	20010830
EP 1313863	A2	WO 2001-US26926	20010830
JP 2004526408	W	WO 2001-US26926	20010830

JP 2004526408 W

JP 2002-523957 20010830

## FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 2001086896 A	Based on	WO 2002018443 A
EP 1313863 A2	Based on	WO 2002018443 A
JP 2004526408 W	Based on	WO 2002018443 A

PRIORITY APPLN. INFO: US 2000-653755 20000901

AN 2002-393728 [42] WPIDS

AB WO 2002018443 A2 UPAB: 20050526

NOVELTY - A **purified** or highly pure immunoglobulin (I) with the same specificity as 4G10 monoclonal antibody, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) an isolated recombinant polynucleotide (II) encoding a polypeptide (III) comprising a **light** chain component comprising a fully defined 214 amino acid sequence given in the specification, and a heavy chain comprising a fully defined 454 amino acid sequence given in the specification;

(2) the complement (IV) of (II);

(3) a vector (V) comprising (II);

(4) a recombinant **cell** (VI) comprising (V) and which expresses (III);

(5) an immunosorbent material (VII) comprising (I) and a microporous polymeric substrate;

(6) producing (M1) a **purified** or highly pure immunoglobulin, by inserting a histidine tag sequence to the C-terminal end of the heavy chain component of an immunoglobulin to be **purified** to produce a histidine tagged immunoglobulin, **purifying** the histidine tagged heavy chain polypeptide by **immobilized** metal affinity chromatography under neutral conditions and specifically preventing exposure of the immunoglobulin to acidic pH, and recovering the **purified** histidine tagged highly **purified** immunoglobulin; and

(7) the immunoglobulin (VIII) produced by (M1).

USE - (I) is useful for detecting the presence of phosphotyrosine containing proteins in a sample, by contacting the sample with an immunosorbent material which includes the monoclonal antibodies and testing for reactivity by immunofluorescence, radioimmunoassay, immunoprecipitation, complement fixation, competitive reaction, Western blotting, immunohistochemistry, flow cytometry or enzyme-linked immunosorbent assay (claimed). (I) is useful in biological/medical research, in diagnosis of a variety of diseases including cancers, to identify **cellular** substrates for tyrosine kinases, affinity **purification** of phosphotyrosine-proteins and for determining the tyrosine phosphorylation status of one or multiple proteins in a given **cell** or tissue sample.

L20 ANSWER 14 OF 19 WPIDS COPYRIGHT 2006 THE THOMSON CORP on STN

ACCESSION NUMBER: 2002-206219 [26] WPIDS

CROSS REFERENCE: 2002-188733

DOC. NO. CPI: C2002-063239 [26]

DOC. NO. NON-CPI: N2002-157036 [26]

TITLE: **Methods** for detecting one or more non-nucleic acid analytes using fusion polypeptides with specificity for the analyte, where the polypeptide comprises first and second inactive functional domains and an analyte

binding domain  
 DERWENT CLASS: B04; D16; S03  
 INVENTOR: DAVIS S C; KREBBER C; MINSHULL J; RAILLARD S A; VOGEL K;  
 WELCH M  
 PATENT ASSIGNEE: (MAXY-N) MAXYGEN INC  
 COUNTRY COUNT: 95

## PATENT INFO ABBR.:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN IPC
WO 2002010750	A2	20020207	(200226)*	EN	159[7]	
AU 2001079135	A	20020213	(200238)	EN		
US 20020127623	A1	20020912	(200262)	EN		
EP 1373889	A2	20040102	(200409)	EN		
AU 2001279135	A8	20051013	(200611)	EN		

## APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2002010750	A2	WO 2001-US24182	20010731
US 20020127623	A1 Provisional	US 2000-222056P	20000731
US 20020127623	A1 Provisional	US 2000-244764P	20001031
AU 2001079135	A	AU 2001-79135	20010731
EP 1373889	A2	EP 2001-957383	20010731
US 20020127623	A1	US 2001-920607	20010731
EP 1373889	A2	WO 2001-US24182	20010731
AU 2001279135	A8	AU 2001-279135	20010731

## FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 2001079135	A	WO 2002010750 A
EP 1373889	A2	WO 2002010750 A
AU 2001279135	A8	WO 2002010750 A

PRIORITY APPLN. INFO: US 2000-244764P 20001031  
 US 2000-222056P 20000731  
 US 2001-920607 20010731

AN 2002-206219 [26] WPIDS

CR 2002-188733

AB WO 2002010750 A2 UPAB: 20050525

NOVELTY - **Methods** for detecting one or more non-nucleic acid analyte (NAA) using fusion polypeptides with specificity for the analyte, where the polypeptide comprises a first inactive functional domain, an analyte binding domain and a second inactive functional domain, are new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are included for the following:

(1) a **method** (M1) for detecting one or more NAA, comprising:

(a) providing at least one fusion polypeptide (P1) with specificity for a NAA, where P1 comprises a first inactive functional domain, an analyte binding domain, and a second inactive functional domain, where binding of the NAA results in a conformational change which brings the first inactive functional domain and the second inactive functional domain into proximity, therefore converting the first and second inactive functional domains into an optically detectable functional domain;

(b) contacting P1 with a sample comprising the NAA; and

(c) detecting the conformational change induced by binding of the NAA, where the NAA is selected from a small organic molecule, a peptide, a polypeptide and a dissolved gas;

(2) another **method** (M2) for detecting one or more NAA, comprising:

(a) step (a) of M1, where the first and second inactive functional domains are converted into a catalytic functional domain;

(b) providing a substrate for the catalytic functional domain;

(c) contacting the fusion polypeptide with a sample comprising the analyte; and

(d) detecting the conversion of the substrate to a product;

(3) another **method** (M3) for detecting one or more NAA, comprising:

(a) providing at least one polypeptide with specificity for a NAA, where the polypeptide comprises an analyte binding domain and a catalytic domain, where binding of the analyte results in an allosteric conformational change which activates the catalytic domain resulting in conversion of a substrate to a detectable product; and

(b) providing a substrate for the catalytic domain;

(c) contacting the polypeptide with a sample comprising the analyte; and

(d) detecting the product produced by activity of the catalytic domain on the substrate;

(4) a **method** (M4) for detecting an analyte, comprising providing at least one biopolymer which undergoes a conformational change upon binding to an analyte, contacting a sample comprising the analyte to the biopolymer; and detecting the conformation change induced by binding of the analyte, where the analyte is not an ion;

(5) a **method** (M5) for identifying a physiologic state, comprising providing at least one biopolymer which biopolymer undergoes a conformational change upon binding to a marker associated with a physiologic state, contacting the biopolymer with a biological sample comprising the marker, and detecting the conformation change induced by binding of the marker, thereby identifying the physiologic state associated with the marker;

(6) a biosensor comprising:

(a) a support; and

(b) at least one polypeptide with specificity for a NAA, where the polypeptide comprises an analyte binding domain and a catalytic domain, where binding of the analyte results in an allosteric conformational change which activates the catalytic domain resulting in conversion of a substrate to a detectable product, where the polypeptide is **immobilized** on the support; or

(c) at least one fusion polypeptide with specificity for a NAA, where the polypeptide comprises a first inactive functional domain, and analyte binding domain, and a second inactive functional domain, where binding of the analyte brings the first inactive functional domain and the second inactive functional domain into proximity, thereby converting the first and second inactive functional domains into a functional catalytic or optically detectable domain where the fusion polypeptide is **immobilized** on the support; or

(d) a polypeptides **immobilized** on the solid support, where the polypeptides having different analyte binding specificities, and a detection system;

(7) a **method** (M6) of sensing one or more test stimulus, comprising:

(a) providing a library of biopolymers comprising nucleic acid variants or expression products of the nucleic acid variants;

(b) arraying the library in a spatial or logical format to provide a physical or logical array;

(c) contacting one or more calibrating stimulus to the array, where one or more members of the array produce one or more detectable signals in response to contact by the one or more calibrating stimulus, thereby producing a calibrating array pattern which identifies contact of the array by the one or more calibrating stimulus;

(d) contacting at least one test stimulus to the array, thereby producing a test stimulus array pattern; and

(e) comparing the test stimulus array pattern to the calibrating array pattern, thereby identifying the test stimulus;

(8) a **method** (M7) of using a re-usable array of biopolymers, comprising:

(a) providing a physical or logical array of biopolymers comprising nucleic acid variants or expression products of the nucleic acid variants;

(b) contacting the physical or logical array with one or more first stimulus;

(c) observing a first resulting response of the array, or collecting a first product resulting from contact between the array and the first stimulus;

(d) reusing the array by contacting the array a second time with the first stimulus, or with a second stimulus, and observing a second resulting response of the array, or collecting a second product resulting from contact between the array and the first or second stimulus, and, optionally, comparing the first resulting response of the array to the second resulting response of the array;

(9) a biopolymer array produced by M6 or M7; and

(10) a computer comprising a data set corresponding to the labeling biopolymer sensor array pattern or test biopolymer sensor array pattern of M6 or M7.

USE - The **methods** and biosensors are useful for detecting a wide range of biological, chemical and biochemical stimuli, e.g. polypeptides, hormones, metabolite and small molecules. They are useful in medical, environmental and industrial diagnostic procedures, for e.g. the array can be used for detection of protein biomarkers associated with disease or other physiological condition.

L20 ANSWER 15 OF 19 WPIDS. COPYRIGHT 2006 THE THOMSON CORP on STN  
 ACCESSION NUMBER: 2002-155051 [20] WPIDS  
 DOC. NO. CPI: C2002-048577 [20]  
 DOC. NO. NON-CPI: N2002-117842 [20]  
 TITLE: Combination of capture agents used as tools for sorting proteins containing polypeptide tags for which the capture agents are specific  
 DERWENT CLASS: B04; D16; S03  
 INVENTOR: AULT-RICHE D; KASSNER P D  
 PATENT ASSIGNEE: (AULT-I) AULT-RICHE D; (KASS-I) KASSNER P D; (POIN-N) POINTILLISTE INC  
 COUNTRY COUNT: 95

# PATENT INFO ABBR.:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN IPC
WO 2002006834	A2	20020124	(200220)*	EN	159[19]	
AU 2001078968	A	20020130	(200236)	EN		
US 20020137053	A1	20020926	(200265)	EN		
EP 1301632	A2	20030416	(200328)	EN		
US 20030143612	A1	20030731	(200354)#	EN		
JP 2004504607	W	20040212	(200413)	JA	407	

# APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2002006834	A2	WO 2001-US22821	20010718
US 20020137053	A1 Provisional	US 2000-219183P	20000719
AU 2001078968	A	AU 2001-78968	20010718
EP 1301632	A2	EP 2001-957199	20010718
US 20020137053	A1	US 2001-910120	20010718
US 20030143612	A1 Div Ex	US 2001-910120	20010718
EP 1301632	A2	WO 2001-US22821	20010718
JP 2004504607	W	WO 2001-US22821	20010718
JP 2004504607	W	JP 2002-512691	20010718
US 20030143612	A1	US 2002-341226	20021227

## FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 2001078968	A	WO 2002006834 A
EP 1301632	A2	WO 2002006834 A
JP 2004504607	W	WO 2002006834 A

PRIORITY APPLN. INFO: US 2000-219183P 20000719  
 US 2001-910120 20010718  
 US 2002-341226 20021227

AN 2002-155051 [20] WPIDS

AB WO 2002006834 A2 UPAB: 20060118

NOVELTY - A combination comprising: capture agents which specifically bind to a polypeptide; and

oligonucleotides that comprise a sequence that encodes a preselected polypeptide to which the agents bind, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

- (1) a set of oligonucleotides (I) comprising the formula 5'-Dn-Em-3';
- (2) a combination of sets of oligonucleotides of defined formulae;
- (3) a system for sorting collections of molecules;
- (4) arrays comprising a support for linking capture agents;
- (5) creating a tagged library (M1) comprising incorporating each one of the set of oligonucleotides of formula (I) into a nucleic acid molecule in a library of nucleic acid molecules to create a tagged library;
- (6) a tagged library.
- (7) screening (M1) a nucleic acid library comprising:
  - (a) translating the library prepared by (M1);
  - (b) contacting proteins from the translated library or sublibrary with a collection of capture agents to produce complexes between the tagged proteins and identifiable capture agents;
  - (c) screening the complexed capture agents to identify those that have bound to a translated protein of interest, therefore identifying the Em that is linked to the protein of interest; and
  - (d) isolating the nucleic acid molecules of the Em linked to the protein of interest.
- (8) a **method** (M2) of nested sorting comprising:
  - (a) creating tagged collections of nucleic acid molecules by incorporating each one of (I) at one end of each nucleic acid molecule to create a master collection comprising N members;
  - (b) amplifying each of n samples with a primer that comprises a single Dn and all of the Em's;
  - (c) translating each sample;

(d) contacting proteins from each translated reaction with one of n collections of capture agents to produce complexes where each of the capture agents in the collection specifically reacts with a sequence of amino acids encoded by an Em, and each of the antibodies can be identified;

(e) screening the complexes to identify those that have bound to a protein of interest, thereby identifying the Em and Dn that is linked to nucleic acid molecules that encode the protein of interest; and

(9) a collection of molecules where each molecule is labelled with one of a set of epitope tags which include a divider region selected from n divider regions and an epitope region that is selected from among m epitopes and where each divider region contains at least three amino acids and where each epitope region contains a sufficient number of amino acids to constitute an epitope to which an antibody can specifically bind.

(10) sorting nucleic acid libraries comprising:

(a) linking a sequence of nucleotides that encodes an epitope to members of a nucleic acid library;

(b) translating the library to produce the encoded proteins with linked epitope tags;

(c) contacting the translated library with linked epitope tags with a collection of capture agents that specifically bind to the epitopes.

D = a unique sequence among the set of oligonucleotides and contains at least 10 oligonucleotides;

E = encodes a sequence of amino acids that comprises an epitope unique in the set and to whose sequence the capture agent will bind;

n and m = an integer of 2 or higher.

USE - The anti-tag capture agents are used as tools for sorting proteins containing polypeptide tags for which the capture agents are specific and for a process of nested sorting. The agents are useful for functional surveys of large diversity libraries such as gene libraries (all claimed).

L20 ANSWER 16 OF 19 WPIDS COPYRIGHT 2006 THE THOMSON CORP on STN  
 ACCESSION NUMBER: 2001-541652 [60] WPIDS  
 CROSS REFERENCE: 2000-431666  
 DOC. NO. CPI: C2001-161708 [60]  
 TITLE: Determining the sequence of a polynucleotide for detection of, diagnosis of or prognosis of disease i.e. cancer and Alzheimer's disease  
 DERWENT CLASS: B04; D16  
 INVENTOR: JARVIK J W  
 PATENT ASSIGNEE: (JARV-I) JARVIK J W; (SEQU-N) SEQUEL GENETICS INC  
 COUNTRY COUNT: 92

#### PATENT INFO ABBR.:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN IPC
WO 2001061028	A2	20010823	(200160)*	EN	64[0]	
AU 2001041522	A	20010827	(200176)	EN		
US 20020155445	A1	20021024	(200273)	EN		

#### APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2001061028	A2	WO 2001-US5058	20010216
US 20020155445	A1 CIP of	WO 1999-US30104	19991216
US 20020155445	A1 Provisional	US 2000-182816P	20000216
US 20020155445	A1 Provisional	US 2000-189310P	20000314



AU 2001041522 A  
US 20020155445 A1

AU 2001-41522 20010216  
US 2001-788268 20010216

## FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 2001041522 A	Based on	WO 2001061028 A

PRIORITY APPLN. INFO: US 2000-189310P 20000314  
US 2000-182816P 20000216  
WO 1999-US30104 19991216  
US 2001-788268 20010216

AN 2001-541652 [60] WPIDS

CR 2000-431666

AB WO 2001061028 A2 UPAB: 20050526

NOVELTY - Determining, (D1), the sequence of a polynucleotide comprising providing a nucleic acid fragment, (F), having a homology of a known reference sequence, (RF), expressing at least one polypeptide, (P), from it and assessing at least one physical property of at least one P to determine the sequence of F, by comparing a property to the predicted properties of a P encoded by RF, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are included for the following:

- (1) genetic analysis comprising D1;
- (2) assessment of a disease;
- (3) assessment of a disease, condition, genotype or phenotype comprises D1 and correlating the determined sequence with the disease, condition, genotype or phenotype;
- (4) diagnostic or prognostic test for a disease, condition, genotype or phenotype comprises D1;
- (5) assessment of a disease, condition, genotype or phenotype;
- (6) diagnosis or prognosis of a disease, condition, genotype or phenotype;
- (7) a data structure useful for detecting and analyzing DNA polymorphisms;
- (8) a computer storage medium;
- (9) a computer implemented **method** to identify an F encoding P, where F is a fragment of RF. The F is of known RF.
- (10) a relational data set is useful for detecting and analyzing DNA mutations and polymorphisms;
- (11) a computer program for searching for the data set of (10);
- (12) genetic analysis comprising;
  - (i) providing two or more nucleic acids samples derived from two or more heterogeneous biological samples;
  - (ii) expressing polypeptides from each nucleic acid sample;
  - (iii) subjecting P, in combination, to physical property assessment; and
  - (iv) comparing the results of the physical property assessment to the predicted properties encoded in at least one RF; and
- (13) providing a nucleic acid molecule.

USE - The **method**, D1, has application for the detection of, diagnosis or prognosis of genetic disease. The diseases include Alzheimer's disease, Ataxia talangietasia, familial adenomatous polyposis, hereditary breast and ovarian cancer, HNPCC, retinoblastoma, Wilm's tumor, Li-Fraumeni syndrome, endocrine neoplasia, Von Hippel-Lindau syndrome, congenital adrenal hyperpalsia, androgen receptor deficiency, tetrhydrobiopterin deficiency, X-linked agammaglobulinemia, Cystic Fibrosis, diabetes, muscular dystrophy, Factor X deficiency, mitochondrial gene deficiency and Factor VII deficiency. The loci include ATM, APC,

BRCA1, BRCA2, CDK2, CDKN2, hMSH2, hMLH1, hPMS1, hPMS2, RB1, WT1, p53, MEN1, MEN2, VHL, CFTR, DMD, BMD and RP.

L20 ANSWER 17 OF 19 WPIDS COPYRIGHT 2006 THE THOMSON CORP on STN  
 ACCESSION NUMBER: 2001-182730 [18] WPIDS  
 DOC. NO. CPI: C2001-054468 [18]  
 DOC. NO. NON-CPI: N2001-130464 [18]  
 TITLE: New recombinant antibody derivative of monoclonal antibody S19, useful as a reagent for **purifying** or detecting human spermatozoa, as an active ingredient of a spermistatic agent, or as a component of a spermicidal contraceptive  
 DERWENT CLASS: B04; D16; S03  
 INVENTOR: DIEKMAN A B; HERR J C; NORTON E J  
 PATENT ASSIGNEE: (UYVI-N) UNIV VIRGINIA PATENT FOUND  
 COUNTRY COUNT: 91

## PATENT INFO ABBR.:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN IPC
WO 2001007083	A1	20010201	(200118)*	EN	48[3]	
AU 2000062278	A	20010213	(200128)	EN		

## APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2001007083	A1	WO 2000-US19843	20000721
AU 2000062278	A	AU 2000-62278	20000721

## FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 2000062278	A	Based on WO 2001007083 A

PRIORITY APPLN. INFO: US 1999-145512P 19990723

AN 2001-182730 [18] WPIDS

AB WO 2001007083 A1 UPAB: 20050525

NOVELTY - A recombinant antibody capable of specifically binding to sperm agglutination antigen-1 (SAGA-1) is new. The recombinant antibody comprises two peptide fragments of the S19 antibody and the fragments are joined together by a linker.

DETAILED DESCRIPTION - The recombinant antibody comprises:

(a) an antibody capable of specifically binding to SAGA-1, comprising two peptide fragments of monoclonal antibody S19 or its peptide mimetics, where the fragments are covalently linked together by a linker, and the recombinant antibody contains less than 30% of the native S19 protein sequences;

(b) a monoclonal antibody comprising an antigen-binding region of the S19 monoclonal antibody, where the antigen-binding region consists essentially of two binding peptides covalently bound to one another by a peptide linker, the binding peptides having an amino acid sequence of:

(i) 116 amino acids (I) and 118 amino acids (II), respectively; or  
 (ii) amino acid sequences identical to (I) or (II), but having 1-3 conservative amino acid substitutions in each of the sequences; or

(c) a recombinant antibody derivative of monoclonal Antibody S19 comprising the biologically active fragments of antibody S19 or its peptide mimetics, where at least 75% of the original S19 protein sequence

has been deleted and the recombinant antibody retains its specificity for the SAGA-1 antigen.

INDEPENDENT CLAIMS are also included for the following:

- (1) nucleic acid sequences comprising:
  - (a) sequences encoding the recombinant antibody;
  - (b) a single chain Fv fragment that consists of:
    - (i) a DNA sequence having 348 base pairs (bp) (III) given in the specification;
    - (ii) a nucleic acid linker; and
    - (iii) a DNA sequence having 354 bp (IV) given in the specification; where the linker is covalently linked to (III) and (IV) so that the expression of the nucleic acid sequence produces a functional Fv fragment; or
  - (c) a single chain Fv fragment selected from:
    - (i) a fully defined DNA sequence having 792 bp (V) obtained from *Mus musculus*;
    - (ii) a fully defined 792 bp DNA sequence (VI), which is a synthetic sequence substituting bacterial codons for mouse codons; or
    - (iii) a fully defined 253 bp DNA sequence (VII), which is a synthetic sequence substituting human codons for mouse codons;
- (2) compositions comprising: (a) as an active agent the recombinant monoclonal antibody in a pharmaceutical carrier; (b) the recombinant monoclonal antibody **immobilized** on a solid support;
- (3) a **method** of detecting the presence of sperm in a biological sample comprising contacting the sample with the composition of (2b) and washing the solid support to remove nonspecifically bound material; and
- (4) a host **cell** comprising heterologous DNA encoding a single chain Fv fragment having a sequence selected from (V), (VI) or (VII).

ACTIVITY - Spermicidal; spermistatic.

No clinical details given.

MECHANISM OF ACTION - Sperm inhibitor.

USE - The recombinant monoclonal antibodies are useful in a passive immunity composition for contraception as they inhibit the ability of sperm to fertilize an egg (claimed) e.g. as an active ingredient of a spermistatic agent, or as a component of a spermicidal contraceptive.

The recombinant monoclonal antibodies are also useful in diagnostic applications, as a reagent for **purifying** and/or detecting human spermatozoa.

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 ACCESSION NUMBER: 2000-602356 [57] WPIDS  
 DOC. NO. CPI: C2000-180346 [57]  
 DOC. NO. NON-CPI: N2000-445671 [57]  
 TITLE: **Purification** of anti-thyroglobulin antibodies from a biological fluid comprises using affinity chromatography with thyroglobulin as the **immobilized** antigen  
 DERWENT CLASS: B04; D16; S03  
 INVENTOR: CORVO L; LOTZ H; SALABE G B; SALABE--ACUTE-- G B  
 PATENT ASSIGNEE: (CNDR-C) CONSIGLIO NAZ DELLE RICERCHE  
 COUNTRY COUNT: 19

PATENT INFO ABBR.:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN IPC
WO 2000058343	A1	20001005	(200057)*	EN	12	[0]
IT 1305309	B	20010504	(200223)	IT		

## APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2000058343	A1	WO 2000-IT116	20000331
IT 1305309	B	IT 1999-RM200	19990331

PRIORITY APPLN. INFO: IT 1999-RM200 19990331

AN 2000-602356 [57] WPIDS

AB WO 2000058343 A1 UPAB: 20050411

NOVELTY - A new process for the **purification** of anti-thyroglobulin antibodies from a biological fluid or its fraction comprises using affinity chromatography with thyroglobulin as the **immobilized** antigen.

DETAILED DESCRIPTION - A new process for the **purification** of anti-thyroglobulin antibodies from a biological fluid or its fraction comprises using affinity chromatography with thyroglobulin as the **immobilized** antigen.

The process comprises:

(a) incubating, under bonding enabling conditions, the biological liquid or its fraction with an effective amount of thyroglobulin bound to a solid support;

(b) washing the solid support under conditions not dissociating the bond between thyroglobulin and anti-thyroglobulin antibodies; and

(c) eluting the anti-thyroglobulin antibodies with an acid pH buffer.

An INDEPENDENT CLAIM is included for an immunological diagnostic kit for the quantitative analysis of anti-thyroglobulin antibodies from serum, where the kit comprises standard anti-thyroglobulin antibodies obtained using the above process.

USE - The process is useful for **purifying** anti-thyroglobulin antibodies from human serum. The anti-thyroglobulin antibodies obtained are useful as standards for quantitative analysis of anti-thyroglobulin antibodies in the human serum (claimed).

The anti-thyroglobulin antibodies are also suitable for structural and functional studies aiming at the identification of sub-class composition of the clone spectrototype and idiotype characteristics. They are also useful in studies of auto-antigene structure of thyroglobulin and cytotoxic effect mechanisms on the thyroid **cell**.

The antibodies are also useful in immunoscintigraphy and immunotherapy to detect or reach thyroid differentiated carcinoma metastasis which **secrete** thyroglobulin but are not able to pick up iodine.

The antibodies are also useful in clinical chemistry and immunometry to obtain a stable derivative from human gamma-globulins to be included in commercial kits for the determination of anti-thyroglobulin antibodies.

ADVANTAGE - The **method purifies** the anti-thyroglobulin antibodies easily and in large amounts. The antibodies obtained by the process are used as highly reliable standards in quantitative determination of anti-thyroglobulin antibodies in the human serum.

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ACCESSION NUMBER: 2000-572269 [53] WPIDS

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DOC. NO. NON-CPI:

N2000-423324 [53]

TITLE:

New isolated antibody for use in compositions and  
**methods** for the diagnosis and treatment of  
 neoplastic **cell** growth and proliferation in  
 mammals, including humans, and in monitoring tumor  
 treatment

DERWENT CLASS:

B04; D16; S03

INVENTOR:

BAKER K P; DESAUVAGE F J; GODDARD A; GURNEY A L; KLEIN R  
 D; ROY M A; WOOD W I

PATENT ASSIGNEE:

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AB WO 2000053754 A1 UPAB: 20060202

NOVELTY - An isolated antibody (Ab) that binds to one of the polypeptides (P) designated PRO213, PRO1330, PRO1449, PRO237, PRO324, PRO351, PRO362, PRO615, PRO531, PRO538, PRO3664, PRO618, PRO772, PRO703, PRO792 or PRO474, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

- (1) a composition of matter comprising Ab;
- (2) a nucleic acid encoding Ab;
- (3) producing an antibody that binds to (P) comprising culturing (15);
- (4) an antagonist of (P);
- (5) a nucleic acid that hybridizes to a nucleic acid sequence encoding (P) or a complement;
- (6) determining the presence of (P) in a sample comprising exposing the sample to anti-(P) antibody and determining binding;
- (7) diagnosing tumor in a mammal comprising:
  - (a) detecting the level of expression of a gene encoding (P) in a test sample of tissue **cells** obtained from the mammal and in a control sample of normal tissue **cells** of the same **cell** type, where a higher expression level in the test sample compared to the control, is indicative of the presence of a tumor; or
  - (b) contacting an anti-(P) antibody with a test sample of tissue **cells** and detecting formation of a complex between the antibody and (P), where formation of the complex is indicative of a tumor in the mammal;
- (8) a cancer diagnostic kit comprising an anti-(P) antibody;
- (9) inhibiting the growth of tumor **cells** comprising exposing **cells** that express (P) to an agent that inhibits the activity or expression of (P);

(10) an article of manufacture comprising a composition containing an active agent that inhibits the growth of tumor **cells** in a container and a label on the container indicating that the composition can treat conditions characterized by overexpression of (P) in tumor **cells** compared to normal **cells** of the same tissue type;

(11) identifying a compound that inhibits a biological or immunological activity of (P) comprising:

(a) contacting a candidate compound with (P) and determining activity inhibition; or

(b) contacting **cells** and a compound to be screened in the presence of (P) to allow induction of a **cellular** response normally induced by (P) and determining induction, where lack of induction indicates the compound is an antagonist;

(12) identifying a compound that inhibits the expression of (P) in **cells** comprising contacting the **cells** with a candidate compound and determining if expression is inhibited;

(13) a nucleic acid that is 80 percent identical to:

(a) a sequence that encodes one of 16 amino acid sequences (S1), given in the specification;

(b) one of 16 nucleotide sequences (S2), given in the specification; or

(c) the full-length coding sequence of the DNA deposited under American Type Culture Collection (ATCC) accession number 209791, 203242, 203243, 209855, 209718, 209784, 209620, 209811, 209702, 209752, 209751, 209813, 209809, 209716, 209846, or 209865;

(14) vectors comprising (2) and (13);

(15) host **cells** comprising (14);

(16) producing (P) comprising culturing (15);

(17) a polypeptide:

(a) with 80 percent identity to one (S1);

(b) scoring 80 percent positives compared to one of (S1);

(c) with 80 percent identity to an amino acid encoded by the full-length coding sequence of DNA deposited under ATCC accession number 209791, 203242, 203243, 209855, 209718, 209784, 209620, 209811, 209702, 209752, 209751, 209813, 209809, 209716, 209846, or 209865;

(18) a chimeric molecule comprising (17) fused to a heterologous amino acid sequence;

(19) an antibody that binds (17);

(20) a nucleic acid 80 percent identical to a sequence encoding a polypeptide of (S1), lacking its signal peptide or a sequence encoding an **extracellular** domain of a polypeptide of (S1), with or lacking its signal peptide; and

(21) a polypeptide 80 percent identical to a polypeptide of (S1) lacking its signal peptide or an **extracellular** domain of a polypeptide of (S1), with or lacking its signal peptide.

ACTIVITY - Cytostatic; antiinflammatory; immunomodulatory. No biological data is given.

MECHANISM OF ACTION - None given.

USE - Ab is used in compositions and **methods** for the diagnosis and treatment of neoplastic **cell** growth and proliferation in mammals, including humans (claimed). Genes and polypeptides encoded by them, that are amplified in the genome of a tumor **cell**, can be identified and are useful targets for the treatment and prevention of certain cancers and may be used to monitor tumor treatment. Compounds that inhibit the expression or activity of the identified polypeptides can be identified and used as antagonists. Benign or malignant tumors, inflammatory disorders and immunological disorders can be treated.

